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ANNALS of SURGERY

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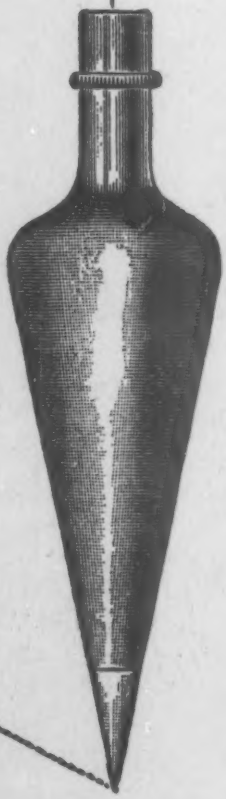

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THE SURGICAL THERAPEUTIC SIGNIFICANCE OF THE FUNCTIONAL BEHAVIOR OF THYROID NODULES*

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THE EXACT FUNCTION of thyroid nodules or adenomas has not been completely established in spite of much work which has been done in an attempt to elucidate the problem. Most of the nodules are believed to originate from an abnormal hyperplasia-involution cycle.[1, 2] However, there are two schools of thought regarding the origin of the so-called fetal adenoma. One group, including Beck,[3] Wölfler,[4] Ribbert,[5] and others, contends that fetal adenoma arises from multiple embryonal cell nests scattered through the thyroid tissue. On the other hand, according to the hypothesis of Virchow,[6] Hitzig,[7] Michaud,[8] and others, which has been preferred by many modern workers, the fetal adenoma develops from the normal adult thyroid epithelium. Some even have postulated that the fetal adenoma is a growth of small acini into preëxisting colloid of a follicle.[9] At times it is difficult to differentiate between the usual nodule and a fetal adenoma so that investigators have called all these tissues either nodules, adenomatous nodules or adenomas of the thyroid gland. As a matter of fact, Boyd[10] stated that many of the nodules which have been regarded as fetal in type are essentially only varieties of the colloid adenoma, since both may be seen shading into the other in a single section.

When an adenoma of endocrine gland tissue occurs, the tumor in certain instances is known actually to function as secretory tissue, as is noted in the hypoglycemia produced by an adenoma of the islets of Langerhans of the pancreas and the hypercalcemia due to an adenoma of the parathyroid gland. In other endocrine glands, such as the thyroid, it has been questioned as to whether adenomas may also cause symptoms, or whether they exist without producing any manifestations of functional activity. Much thought has also been given to such questions as to whether the nodular or the paranodular goitrous tissue is responsible for the hyperthyroidism in the patient with toxic nodular goiter, as to whether the nodules of nodular goiter are even capable of functioning, and as to why large amounts of adenomatous tissue may often be removed from the patient with nontoxic nodular goiter without producing

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appreciable change in the clinical thyroid function or in the basal rate of metabolism, and from the patient with toxic nodular goiter without producing postoperative hypothyroidism.

A number of pathologists and investigators confusing the parenchymatous appearance of some nodules or of some paranodular tissue with that of hyperactive thyroid tissue in which there is also a predominance of epithelial over colloid material, were led to believe that these nodules were also made of hyperactive thyroid tissue. However, further investigation revealed that the nodules, paranodular tissue, or both may show evidences of hyperplasia in a certain number of cases of nontoxic nodular goiter. We now know that the presence of hyperplasia or hypertrophy cannot be considered a definite criterion of the presence of clinical hyperthyroidism. Johnson,[11] in 1939, reported that 19 per cent of all nodules of nontoxic nodular goiter show hypertrophy and only 37.4 per cent of the nodules of toxic nodular goiter show similar hypertrophy.

The surgeons have also tried to solve this problem by simple enucleation of a so-called hyperfunctioning adenoma. Parsons,[12] of Columbia University, in 1927, and others, have reported amelioration of toxic symptoms after such surgery. At first thought this would indicate that the adenomatous tissue, *per se,* had been the cause of the hyperfunction. On the other hand, Holst,[13] and others, have reported similar dramatic amelioration of the hypothyroid state after enucleation of a single adenoma. Why such patients with hyperthyroidism or hypothyroidism return to a euthyroid state after thyroid surgery still remains unknown. May it be that the adenomatous tissue stimulates the surrounding tissue to hyperfunction in one instance and inhibits it to hypofunction in another instance and with removal of the adenomatous tissue there is amelioration of symptoms? These surgical end-results may also be related to other factors than the surgery, *per se,* perhaps to factors in the preoperative or postoperative care. Furthermore, it should be emphasized that after such simple enucleation the chances for recurrence of the symptoms are greater, as was pointed out years ago by Parsons,[12] so that bilateral subtotal thyroidectomy is now considered the operation of choice by many for at least the usual case of toxic nodular goiter.

Marine[14] reported, in 1912, that fetal, intermediate and simple adenomas contained almost invariably smaller amounts of iodine than the surrounding nontumor thyroid. He did not differentiate toxic from nontoxic goiter. Wegelin[15] later found that adenomatous tissue fed to tadpoles exerted less effect on growth than the surrounding thyroid tissue. Branovacky,[16] also using Gudernatch's tadpole test, found that the tissue from the nodular element in secondary toxic goiter was rather more active than the internodular tissue.

Because methods of determining the functional behavior of various parts of a nodular goiter, heretofore, have been so equivocal and inadequate, we have felt that radioiodine may be of help in solving this problem. Recently, a group of us, Dr. George M. Curtis, Dr. Charles P. Leblond, Miss Elsie Riley, Mrs. Martha Radike, and I, made radioiodine and ordinary iodine fractionation studies[17] of many forms of pathologic thyroid tissue removed from seven patients with various clinical types of goiter and varying degrees of toxicity.

These data indicate that the cells of all types of nodular or adenomatous thyroid tissue thus far studied are functionally autonomous and consistently produce less thyroxine and diiodotyrosine, and show less avidity for iodine than the groups of thyroid cells in the surrounding tissue. The biochemical aspects of the problem have already been set forth.[17] We now wish to present the clinical and surgicopathologic background together with a detailed correlation between the various phases of the work as well as the probable surgical significance of the findings.

EXPERIMENTAL METHODS

During the preoperative period several determinations of the basal metabolic rate were made. Repeated determinations of the acetone-soluble and insoluble iodine fractions of the blood were also carried out. None of these patients received iodine in the immediate preoperative period other than a minimal (two micrograms) given just before operation with the radioiodine solution. Actual preparation of the hyperthyroid patients for thyroidectomy included general measures, such as adequate mental and physical rest, adequate sedation, a well-balanced diet of high carbohydrate, high protein, high vitamin and high caloric content, as well as calcium, phosphorus and vitamin D in sufficient doses and treatment of existing complications.[18] None had received thiouracil. One (L. D.), was known to have received iodine at home up to five weeks prior to operation.

A solution of radioiodine containing 25 to 1,000 microcuries of the radioactive element I^{131} and about 2 micrograms of ordinary iodine I^{127} was administered 15 to 23 hours before thyroidectomy, with the exception of R. G., when 40 hours intervened between the administration and operation. The small iodine content of the solution of radioactive iodine insured that a true picture of the physiologic behavior of iodine would be given by studies with radioiodine.

Blood was drawn during operation (15 to 20 hours after ingestion of radioiodine) from one patient with nontoxic and from one with toxic goiter. This showed no detectable radioiodine in organic combination. We have, therefore, assumed that the radioiodine present in organic combination in each thyroid gland represents a nearly true picture of the ability of that gland to produce physiologically active organic iodine compounds. However, these data are too few and further investigation of this phase of the methods used is necessary.

An idea of the total thyroid weight was gained by recording the weight of the goitrous tissue removed and estimating the amount of thyroid tissue left behind. For study of the nodular goiters we chose large and representative sections of as well-circumscribed nodules as possible which were in appearance quite similar to the other nodules present. A representative portion of the surrounding or paranodular thyroid tissue was also carefully selected for study. A portion of each selected tissue was given to the biochemist for determination of radioactivity and of ordinary iodine. The other portion was serially sectioned for microscopic study.

Determinations of ordinary iodine I^{127} and radioiodine I^{131} were performed in the various iodine fractions of both the nodules and the surrounding thyroid tissue. The inorganic iodine, the diiodotyrosine iodine, and the thyroxine iodine were separated after a method used by Mann, Leblond and Warren.[19] A portion of the solution of each fraction was used to determine iodine I^{127} by a wet ash method,[20] with slight modification. Another portion of the solution was used for measurement of the radioactivity by the Geiger counter. Details of biochemical methods used have already been presented.[17]

The microscopic sections shown are quantitatively the most representative of the serial sections studied.

RADIOACTIVE IODINE INGESTION

Seven patients with various diseases of the thyroid gland were given radioactive iodine by mouth, thyroidectomized, and the removed goiters were investigated grossly, microscopically and biochemically. The protocols may be reviewed briefly as follows:

REVIEWS OF PROTOCOLS

Protocol of M. H.—No. 445260, with Nontoxic Diffuse Colloid Goiter and a Fetal Adenoma: M. H., a colored schoolgirl, age 15, entered University Hospital, June 19, 1944, for surgical treatment of a nodular goiter.

She had enjoyed entirely good health up to about six months ago when she first became aware of a lump in the right neck anteriorly. This gradually grew outward, producing a tumor so unsightly as to lead the patient and her family to request its removal for cosmetic reasons. There were no pressure symptoms related to breathing or swallowing. No toxic symptoms occurred, such as tachycardia, tremor of the fingers or exophthalmos. No known iodine treatment had been given. Measles and mumps occurred in childhood. She had no other illnesses except for frequent sore throat. Past history and inventory by systems were otherwise negative. One sister had goiter.

Physical examination disclosed a well-developed and well-nourished colored girl, age 15, lying quietly in bed in no acute distress. Skin was of normal warmth and moisture. Eyes protruded normally, the exophthalmometric reading being 14 mm. for each eye, which is normal. Few carious teeth were present. The tongue presented no tremor. The oropharynx was clear. The tonsils were slightly enlarged and a few infected follicles were present. Examination of the neck revealed a bilateral, diffuse soft enlargement of the thyroid which was not very marked. However, in the midportion of the right lobe there was also a large hard nodule which felt smooth. It protruded for about two inches, thus constituting a cosmetic blemish. This moved with deglutition. The trachea was in the midline. The extended and abducted fingers showed no tremor.

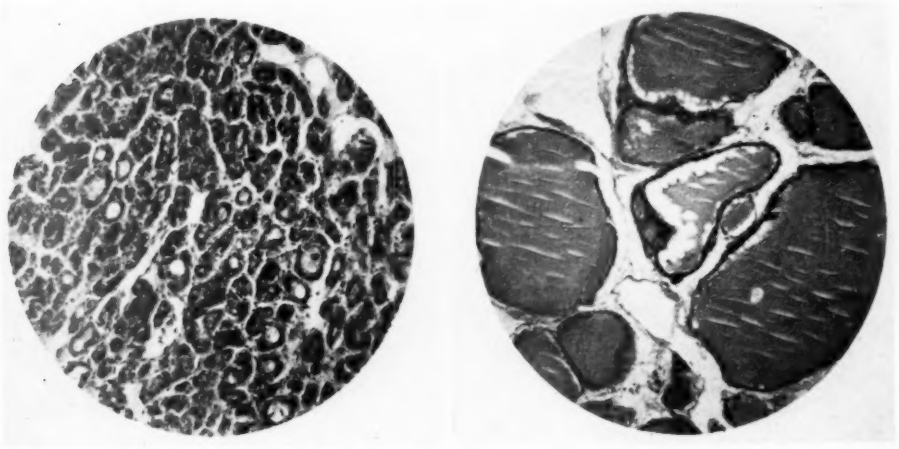
Admission red blood count was 4,300,000, with the hemoglobin 13.6 Gm. per cent. The white blood cell count was 8,400, with neutrophils 60 per cent, lymphocytes 37 per cent, monocytes 1 per cent, and eosinophils 2 per cent. Urinalysis was negative. Blood Mazzini and Kahn reactions were negative. The basal metabolic rate on June 20 was plus 7 per cent, with the temperature 98.4°F., pulse 72, and respirations 12. A basal metabolic rate determination on June 22 was minus 2 per cent, with the temperature 98.2°F., pulse 72, and respirations 19. The total blood iodine averaged 4.88 and the acetone insoluble fraction 1.30 micrograms per cent, which are normal. Fluoroscopy of the chest and neck revealed the trachea in the midline, and no retrotracheal extension of the goiter. No intrathoracic extension was noted. Otherwise, fluoroscopy was negative. Indirect laryngoscopy showed both vocal cords normal in appearance and function.

Radioactive iodine was given in grape juice at 1:00 P.M. on June 22, 1944. Morphine,

gr. ⅛, and scopolamine, gr. 1/300 were given pre-anesthetically. Usual skin preparation was made with tincture of quatresin. Usual draping was carried out.

Under avertin, 80 mg. per kilo per rectum, as well as cyclopropane, oxygen and helium anesthesia, a right partial thyroidectomy was done by one of us (I. D. P.) at 9:00 A.M. on June 23, 1944. The large nodule of the right lobe was removed together with a minimal amount of diffuse tissue. The remaining portions of the thyroid gland were left alone because we felt that this was a manifestation of diffuse goiter occurring in an endemic area during adolescence and that it could be treated adequately by administration of iodine.

The right thyroid lobe as removed measured 4.5 x 3.5 x 3.5 cm., and weighed 18 Gm. It contained one large nodule. On cross-section, the nodule measured 3 cm. in diameter. It was sharply circumscribed and encapsulated by a thin wall of fibrous tissue. It consisted of a fairly solid, light tan material of uniform appearance which contained very little colloid. The extranodular tissue was diffuse in character and on cross-section presented a uniform appearance associated with the presence of an excess amount of colloid. Microscopically (Fig. 1A), the nodule showed a typical fetal adenoma with the acini very



A B

FIG. 1.—(A) Fetal adenoma of thyroid. Note that the follicles are principally tubular in type but some are microfollicular. (x 150)

(B) Paranodular thyroid tissue. Diffuse colloid goiter of adolescence. Note the large size of the follicles and the presence of proliferative changes. (x 150)

small in a few instances and macrofollicular in other areas, but principally tubular in type and the interstitial tissue was small in amount. The tissue surrounding the nodule (Fig. 1B) showed the acini larger than normal and the cells flattened. The colloid was moderately dense and showed very little vacuolation. However, a few areas of hyperplasia consisting of heightening of the cells with layering and plication, were noted here and there throughout the paranodular tissue. *Final Diagnosis:* Diffuse nontoxic colloid goiter with a single fetal adenoma.

The postoperative condition remained excellent. The temperature, pulse and respirations remained normal. The patient was kept in semi-Fowler's position and an ice collar was applied over the dressing. Sips of water were allowed as desired, and food as soon as it could be taken. There was never evidence of parathyroid deficiency or of recurrent laryngeal nerve injury. The wound healed well. Alternate sutures were removed on the second and the remainder on the fourth day. The patient was discharged on the fourth

day, June 27, 1944, as improved. One tablet of oridine (iodine 10 mg.) once daily for 70 days was prescribed.

She was seen in the Out-patient Surgical Clinic on September 11, 1944, at which time she was well and the wound appeared healed and in good condition. She had taken one tablet of oridine (10 mg. of iodine) daily for 70 days. The thyroid, on June 25, 1945, was normal in size and consistency, and the basal metabolic rate was plus one per cent. The patient was then considered cured.

COMMENT.—Twenty hours intervened between the administration of the radioiodine solution and the thyroidectomy. Study of this goiter revealed remarkable differences between the storage of iodine by the fetal adenoma (Fig. 1A) and that by the typical nontoxic diffuse colloid goiter (Fig. 1B) which surrounded the adenoma. The adenoma (Fig. 2 M. H.) contained a

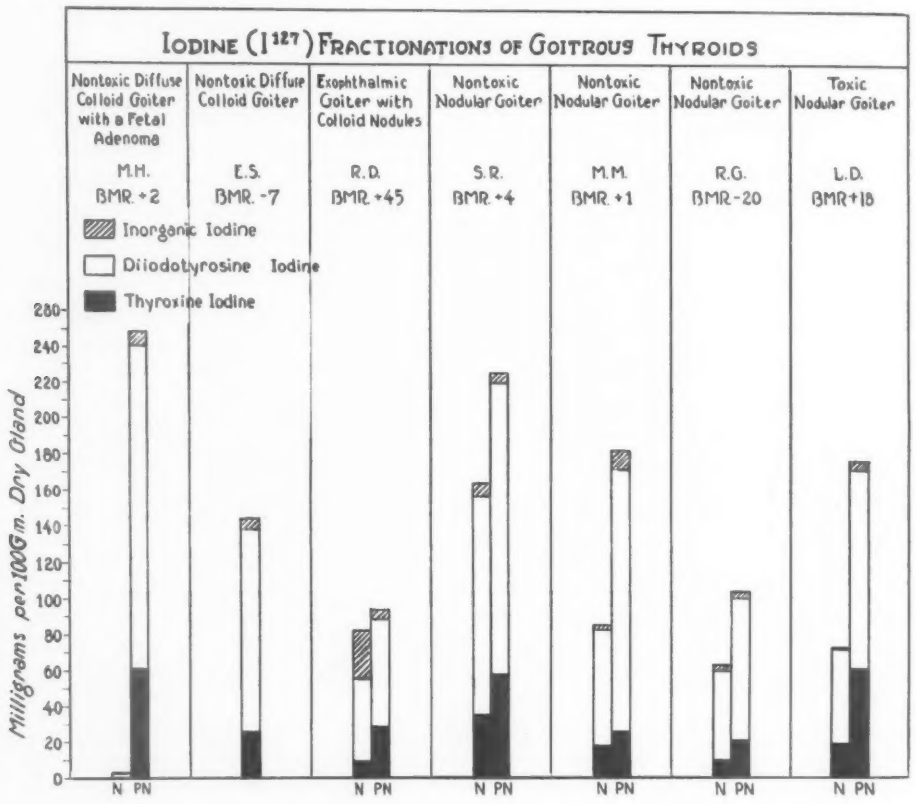


FIG. 2.—N—Nodular thyroid tissue, PN—Paranodular thyroid tissue.

minimum of elemental iodine, 2.7 milligrams per 100 Gm. of the dried gland, of which 1.6 mg. per cent was distributed in the diiodotyrosine fraction, 0.9 mg. per cent in the thyroxin fraction, and 0.4 mg. per cent in the inorganic fraction. This was much less than the figures for the paranodular tissue (Fig. 2 M. H.) which contained 250.0 mg. per cent of elemental iodine I^{127} per 100 Gm. of dried gland of which the diiodotyrosine fraction was largest, 179.0 mg.

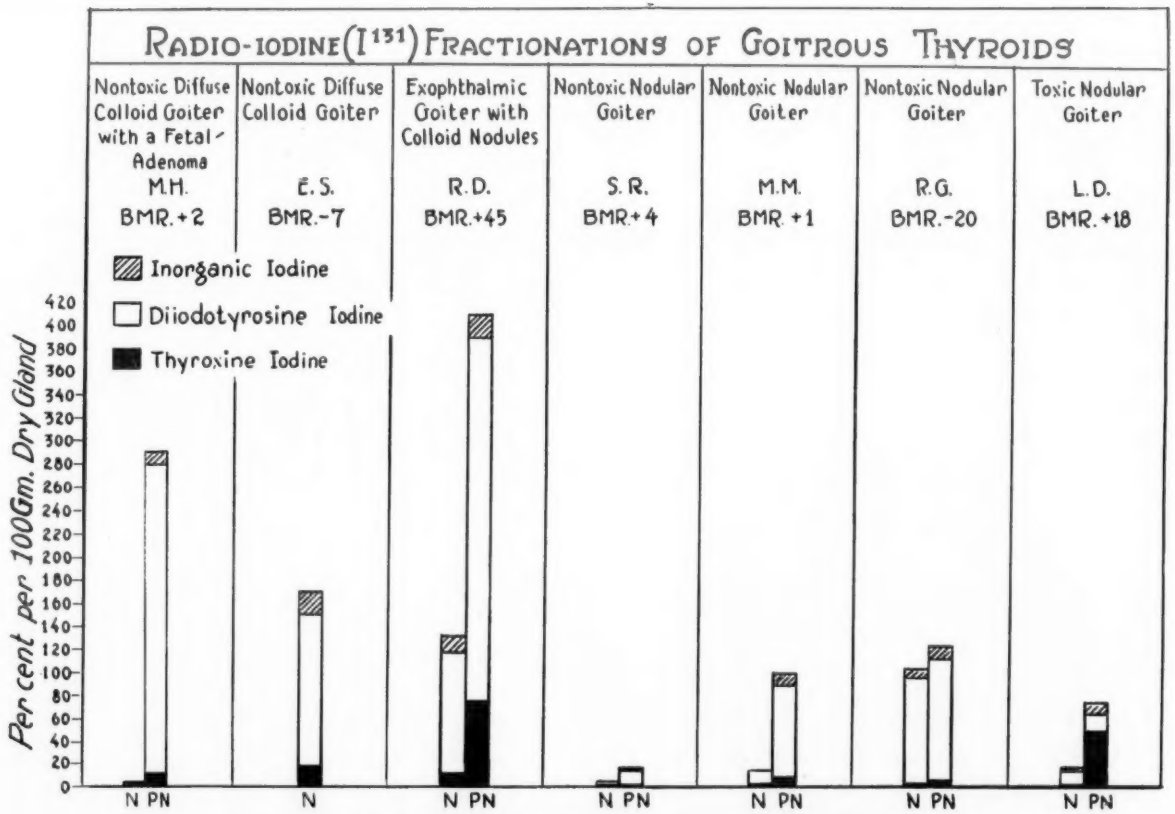


FIG. 3.—N—Nodular thyroid tissue, PN—paranodular thyroid tissue.

per cent, the thyroxine fraction being 63.3 mg. per cent and the inorganic fraction 7.6 mg. per cent.

The nodule (Fig. 3 M. H.) contained a minimum of the radioiodine given 20 hours before thyroidectomy, 2.4 per cent per 100 Gm. of dry gland, of which 1.5 per cent was distributed in the inorganic iodine fraction, 0.9 per cent in the diiodotyrosine and 0.6 per cent in the thyroxine fraction. These figures reveal much less avidity for radioiodine by the fetal adenoma than by the diffuse colloid goiter of adolescence (Fig. 3 M. H.) which contained 195.2 per cent of the radioiodine given per 100 Gm. of dry gland, of which the diiodotyrosine fraction was largest, 267.2 per cent, the thyroxine fraction being 12.9 per cent and the inorganic fraction 8.3 per cent.

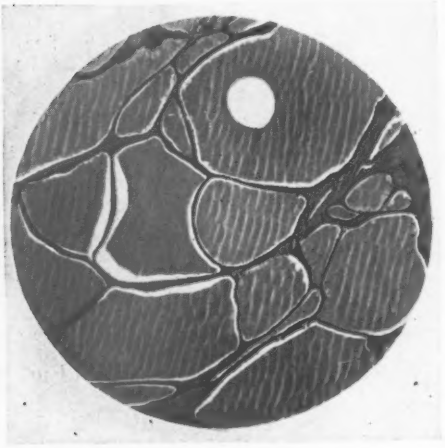


FIG. 4.—Diffuse colloid goiter. The lining epithelium is much flattened, and the colloid is dense and abundant. (x 150)

These figures also demonstrate that the diffuse colloid goiter of adolescence produced much more of the physiologically active organic iodine compounds (thyroxine and diiodotyrosine) than the fetal adenoma which produced minimal amounts.

Protocol of E. S.—No. 445276, with Nontoxic Diffuse Colloid Goiter: E. S., a married colored female, age 27, entered University Hospital, June 20, 1944, for the surgical treatment of goiter.

She first became aware of goiter about three years ago. Except for occasional dysphagia and dyspnea it remained symptomless. The past history was negative except for sickle cell anemia.

Physical examination revealed a well-nourished, colored female, who was quiet. The thyroid was diffusely, symmetrically and moderately enlarged.

Admission red blood count was 5,270,000, with the hemoglobin 14.5 Gm. per cent. There was slight sickling of the red cells. The white blood count was 8,950, with the neutrophils 49 per cent, lymphocytes 46 per cent, monocytes 4 per cent, and eosinophils 1 per cent. The urinalysis was negative. The blood Wassermann and Mazzini tests were negative. The average basal metabolic rate was minus 7 per cent, with the basal pulse 80, respirations 19, temperature 98.2°F., the blood pressure 128/72, and the weight 120 pounds. The total blood iodine averaged 2.70 and the acetone-insoluble fraction 1.02 micrograms per cent, which are normal. The blood urea nitrogen was 13 mg. per cent. Renal function tests were normal. The blood prothrombin was 65 per cent, which is normal. The blood cholesterol was 316 mg. per cent. Roentgenography revealed the trachea displaced to the left.

Radioactive iodine was given in grape juice on July 17, 1944, at 12 noon. No other iodine was given at any time preoperatively.

Bilateral subtotal thyroidectomy was done by one of us (I. D. P.) under avertin, cyclopropane, oxygen and helium anesthesia at 8 A.M. on July 18, 1944. It was followed by an uneventful recovery.

The goiter as removed weighed 59 Gm. About 15 Gm. of thyroid tissue were left

behind. The right thyroid lobe as removed measured 6.5 x 3.5 x 4 cm. The left lobe measured 8 x 3 x 3 cm. The isthmus measured 3 x 4 x 2 cm., and the pyramidal lobe measured 1.5 cm. in diameter. The goiter grossly appeared symmetrically and generally enlarged. An excess amount of colloid was noted on cut-section. Microscopically (Fig. 4), the acini were much larger than normal, the cells were flattened and the colloid was abundant and moderately dense, with few vacuoles. However, a few areas of spur formation were also noted. *Final Surgical Diagnosis:* Nontoxic diffuse colloid goiter.

COMMENT.—There was a 20-hour interval between administration of the radioiodine and the thyroidectomy. This goiter, which was typically diffuse colloid in character (Fig. 4) and nontoxic, contained 163 mg. per cent of elemental iodine I^{127}, of which the diiodotyrosine fraction was largest, 114 mg. per cent, with the thyroxine 25 mg. per cent and the inorganic fraction 3.5 mg. per cent (Fig. 2 E. S.). It showed considerable avidity for radioiodine (Fig. 3 E. S.) comparable to the nontoxic diffuse colloid goiter of adolescence (M. H.) storing 163 per cent per 100 Gm. of dry gland of the radioiodine given 20 hours prior to thyroidectomy. The diiodotyrosine fraction was largest, 137 per cent, the thyroxine fraction being 16 per cent and the inorganic fraction 13 per cent.

This study again demonstrates the increased avidity for iodine (Fig. 3 E. S.) by the nontoxic diffuse colloid goiter and its ability to produce large percentages of physiologically active organic iodine compounds.

Protocol of R. D.—No. 446794, with Exophthalmic Goiter and Three Small Colloid Nodules, Treated Preoperatively without Iodine or Thiouracil: R. D., a colored female, age 39, was admitted to University Hospital, August 1, 1944, for the surgical treatment of exophthalmic goiter.

She had been well up to January, 1944, when severe nervousness occurred. This was accompanied by easy fatigability, muscular weakness, emotional and heat instability, palpitation, exophthalmos, a gradually enlarging goiter and loss of body weight from 142 to 133 pounds in spite of a voracious appetite.

Physical examination revealed a well-developed woman who appeared to have lost weight recently. The facial expression was of frozen terror. Exophthalmometric readings were 20 mm. bilaterally. The thyroid was moderately and diffusely enlarged. There was fine tremor of the extended hands.

Admission red blood count was 4,500,000, with the hemoglobin 13.2 Gm. per cent, and the white blood count 8,300, with the neutrophils 66 per cent, lymphocytes 31 per cent, monocytes 2 per cent and eosinophils 1 per cent. The urinalysis was negative. The blood Wassermann and Mazzini tests for syphilis were negative. The prothrombin was 75 per cent, which is normal. The hippuric acid test of liver function yielded 2.97 Gm. The total blood iodine averaged 18.63 and the acetone insoluble fraction 11.11 micrograms per cent, which are greatly increased.

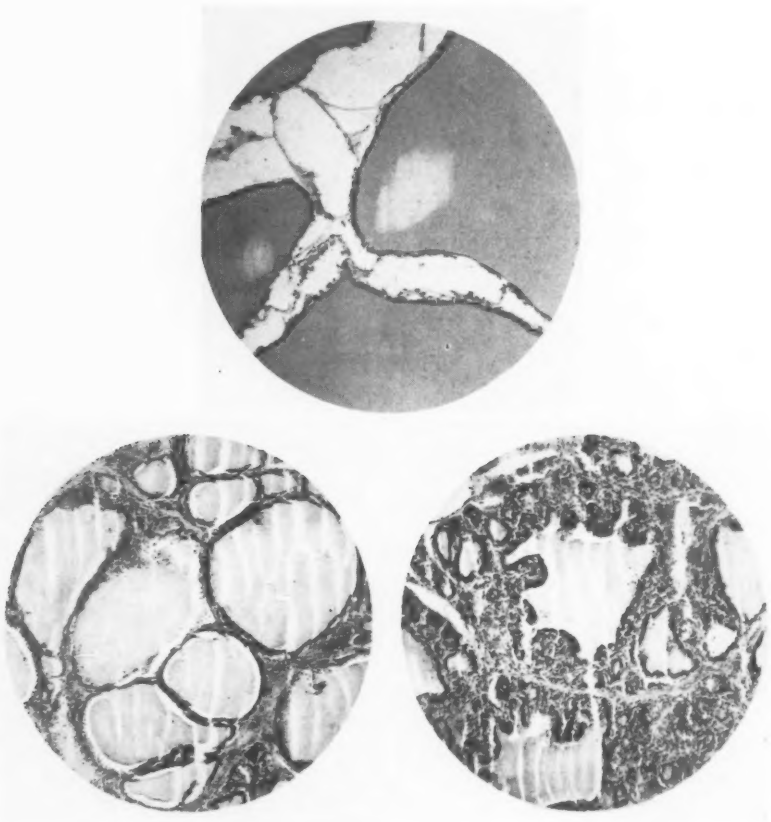
The basal metabolic rate was plus 45 per cent on August 2, 1944, with the basal pulse 96, respirations 23, temperature 98.6°F.; the blood pressure 118/76; and the weight 138 pounds. The patient was prepared in the usual manner for operation except that iodine was omitted. A high caloric, high carbohydrate, high protein, high mineral and high vitamin diet was given. Extra calcium and phosphorus as well as vitamin D were given as two calirad wafers (dicalcium phosphate with viosterol) three times daily. Two capsules of vitamin B complex three times daily, ten milligrams of thiamin chloride three times daily and synkayvite (synthetic vitamin K) were given. Sufficient bed rest was allowed. Adequate sedation with phenobarbital was used. With these methods[18] alone, without use of iodine, the basal metabolic rate decreased to plus 27 per cent on August

14, 1944, with the basal pulse 80; respirations 18; temperature 98°F.; blood pressure 118/74; and the body weight 133 pounds.

Radioactive iodine was given in grape juice on August 14, 1944 at 5:30 P.M. No other iodine was given preoperatively.

Bilateral subtotal thyroidectomy under avertin, cyclopropane, ether, oxygen and helium anesthesia was done by one of us (I. D. P.) on August 15, 1944, at 8:30 A.M., and the postoperative course remained entirely uneventful.

A



B C

FIG. 5.—(A) Typical colloid nodule. (x 150)

(B) Paranodular tissue. There were frequent areas of involution of this exophthalmic goiter gland even though the patient did not receive iodine in the preoperative preparation. (x 150)

(C) Exophthalmic goiter. Much of the goiter consisted of this tissue. Note the tall cells, papillae and vacuoles. (x 150)

The goiter as removed weighed 46 Gm. About 10 Gm. of thyroid were left behind. The right lobe measured 8 x 3 x 3 cm. and weighed 20 Gm. The left lobe and isthmus measured 6.5 x 4 x 3 cm., and weighed 26 Gm. On gross observation the gland appeared diffusely and symmetrically enlarged except for a small cyst containing straw-colored fluid and a small nodule which was observed in the lower pole of the right lobe. The cystic fluid was aspirated for study. On cross-section, the nodule of the right lobe meas-

ured one centimeter in diameter. Cross-section also revealed two small nodules in the lower pole of the left lobe. Each measured about 8 mm. in diameter. The gland otherwise appeared beefy in character and contained a minimum of colloid. The nodule studied was typically colloid in type (Fig. 5A). The paranodular tissue showed areas of hyperplastic tissue characteristic of exophthalmic goiter (Fig. 5C) as well as frequent areas of involution (Fig. 5B).

COMMENT.—The interim between radioiodine administration and thyroidectomy was 15 hours. This patient with exophthalmic goiter received no preoperative iodinization and the biochemical findings are most remarkable.[17b] The paranodular tissue which was typical diffuse hyperplastic goiter (Fig. 5B) with not rare areas of involution (Fig. 5C) showed the least concentration (Fig. 2 R. D.) of elemental iodine I^{127}, 93.96 mg. per cent, of all paranodular tissues studied, and yet its avidity (Fig. 3 R. D.) for radioiodine was tremendous, 410.14 per cent per 100 Gm. of dry thyroid gland, and unsurpassed by any of the thyroid tissues studied. Even though this paranodular tissue (Fig. 2 R. D.) contained small amounts of physiologically active elemental organic iodine compounds, 60.9 mg. per cent diiodotyrosine and 26.9 mg. per cent thyroxine, with the inorganic fraction 6.16 mg. per cent, the markedly increased ability to produce these physiologically active organic iodine compounds (Fig. 3 R. D.) was presented by the high values for the diiodotyrosine radioiodine I^{131} of 313.0 per cent and 76.6 per cent for the thyroxine fraction. The inorganic iodine I^{131} was 20.44 mg. per cent.

The nodular tissue which was typically colloid (Fig. 5A) in character and which was probably only incidentally present also presented significant findings. Its ordinary iodine I^{127} content was smaller (Fig. 2 R. D.) than that of the paranodular tissue, 81.12 mg. per cent, with the diiodotyrosine fraction 45.6 mg. per cent, the inorganic fraction 26.29 mg. per cent and the thyroxine fraction 9.23 mg. per cent. Its avidity for radioiodine (Fig. 3 R. D.) was much greater, 128.55 per cent, than that of the usual nodule, and yet remarkably less than that of the diffuse hyperplastic tissue of exophthalmic goiter, 410.14 per cent. Its ability to produce physiologically active iodine compounds (Fig. 3 R. D.) was also less than that of the paranodular tissue so that the diiodotyrosine was 108.4 per cent, with the thyroxine fraction 10.69 per cent, the inorganic fraction being 9.46 per cent.

Protocol of S. R.—No. 446693, with Nontoxic Nodular Goiter: S. R., a colored housewife, age 54, was admitted to University Hospital, July 30, 1944, for surgical treatment of goiter.

She had had a goiter since the age of 7 years. There were no pressure or toxic symptoms. The goiter was nodular in character and her family physician advised thyroidectomy because of a fear of cancer.

Physical examination presented a well-developed and well-nourished female. A moderately large nodular goiter was present. Indirect laryngoscopy revealed paralysis of the left cord.

Admission red blood count was 4,500,000, with the hemoglobin 13 Gm. per cent. The white blood count was 5,000, with the neutrophils 66 per cent, lymphocytes 32 per cent and monocytes 2 per cent. The urinalysis was negative. The blood Wassermann and Mazzini tests for syphilis were negative. The basal metabolic rate determinations

averaged plus 4 per cent, with the basal pulse 80, respirations 18, temperature 98°F., blood pressure 126/70, and the weight 175 pounds. The total blood iodine averaged 5.82 and the acetone insoluble fraction 1.70 micrograms per cent. The blood urea nitrogen was 14.0 mg. per cent. The hippuric acid test of liver function yielded 3.13 Gm. Roentgenography revealed the trachea in normal position.

Radioiodine was given in grape juice on August 2, 1944, at 3:00 P.M.

Subtotal thyroidectomy was performed by one of us (I. D. P.) on August 3, 1944, at 9:00 A.M., under avertin, cyclopropane, oxygen and helium anesthesia. The postoperative course was uneventful.

The goiter as removed weighed 88 Gm. About 20 Gm. of thyroid tissue was left behind. The right thyroid lobe measured 6 x 3 x 4 cm. Cross-section revealed many colloid nodules, the largest of which measured 3 cm. in diameter. The left thyroid lobe and isthmus as removed measured 9.5 x 3.5 x 5.0 cm. It contained a multiplicity of

A B

FIG. 6.—Nontoxic Nodular Goiter.

(A) Nodule. Note that the small colloid-containing acini are widely separated by a peculiar material, the exact nature of which has not yet been determined. (x 150)

(B) Paranodular tissue. Note the marked interacinar fibrosis and hyalinization and the tendency to accumulation of colloid over normal. (x 150)

nodules of varying size, the smallest measuring 5 mm. and the largest 3.5 cm. A pyramidal lobe which contained nodular tissue was also removed. All lobes revealed evidences of fibrosis, calcification, old hemorrhage, hyaline degeneration and cholesterol deposition. At each upper pole there was a moderate amount of thyroid tissue having a more normal appearance, but even this was the seat of degenerative changes. Microscopically, the nodules studied (Fig. 6A) showed the acini to be widely separated by a peculiar material, the exact nature of which has not been determined. The paranodular tissue (Fig. 6B) was the seat of marked interstitial fibrosis with hyalinization.

COMMENT.—Thyroidectomy was performed 18 hours subsequent to administration of the radioiodine. Both the nodular and paranodular tissues, even though presenting marked evidence of degenerative changes (Fig. 6A and B), revealed an abundance of elemental iodine (Fig. 2 S. R.), 160.2 and 228.0 mg. per cent, respectively, which may indicate that the patient had had iodine at home. Yet the nodular iodine remained lower and its fractions were 123.0 mg. per cent of diiodotyrosine, 34.6 mg. per cent of thyroxine, and 4.5 mg. per cent

of inorganic iodine. It is difficult to conceive that the small amount of colloid within the acini (Fig. 6A) could possibly store so much iodine. It is possible that the large amount of substance which separates the acini may be related to the colloid within the acini and may be able to store an increased amount of iodine. Diiodotyrosine was the largest of the paranodular iodine, 160.0 mg. per cent, the thyroxine fraction being 59.2 mg. per cent and the inorganic fraction 7.1 mg. per cent.

The avidity for radioiodine (Fig. 3 S. R.) was lower than that of all goiters studied, both for the nodular and paranodular tissues, 5.8 and 12.2 per cent, respectively. This may have resulted from decreased function due to the marked pathologic changes shown by both the nodular (Fig. 6A) and paranodular (Fig. 6B) tissues. On the other hand, it may indicate that the tissues had already been saturated by a former iodinization at home, as is also indicated by the high inorganic iodine content of the blood.

Protocol of M. M.—No. 445877, with Nontoxic Nodular Goiter: M. M., a colored housewife, age 60, entered University Hospital, July 6, 1944, for the surgical treatment of goiter.

The patient had become aware of goiter 18 years ago. It remained symptomless up to about four years ago when she experienced dyspnea. Palpitation accompanied during the past few months.

Physical examination presented a tall, obese female in no apparent distress. A large multinodular goiter was easily palpable.

Admission red blood count was 4,520,000, with the hemoglobin 14 Gm. per cent. The white blood count was 7,650, with neutrophils 70 per cent, lymphocytes 26 per cent, monocytes 2 per cent and eosinophils 2 per cent. Urinalysis was negative. The blood Wassermann and Mazzini tests for syphilis were negative. The basal metabolic rate averaged plus 3 per cent with the basal pulse 64, respirations 9, temperature 98.4°F., blood pressure 155/88, and the weight 218 pounds. The total blood iodine was 5.45, and the acetone-insoluble fraction 1.92 micrograms per cent. The blood urea nitrogen was 14.0, and the blood sugar 80 mg. per cent. Phenolsulfonphthalein test of renal function yielded 40 per cent excretion of the dye during the first hour and 15 per cent during the second hour after intravenous administration. The hippuric acid test of liver function yielded 3.54 Gm., which is normal.

Radioactive iodine was given at 7:00 P.M. on July 7, 1944. Subtotal thyroidectomy was performed by one of us (I. D. P.) under avertin, cyclopropane and oxygen anesthesia at 12 noon on July 8, 1944. The postoperative reaction was minimal.

The goiter as removed weighed 206 Gm. It consisted principally of nodular tissue. The paranodular tissue was minimal. About 10 Gm. of thyroid tissue were left behind. The left thyroid lobe and isthmus as removed weighed 200 Gm. and measured 10 x 9 x 5.5 cm. It contained many nodules varying in size from 0.5 to 4 cm. in diameter. Cross-section showed many nodules which were principally colloid in nature but varied greatly in character because of varying degrees of fibrosis and hemorrhage. The nodules were well-circumscribed by fibrous connective tissue. Marked degenerative changes including fibrosis, calcification, hyalinization, cholesterolization and cyst formation were generally present. The right thyroid lobe as removed weighed 6 Gm. It measured 4 x 2 x 1.5 cm. This lobe contained two small nodules measuring 0.5 and 1.0 cm. in diameter, respectively. These were colloid in character. Microscopically, the tissue studied showed marked fibrosis, with hyalinization of the nodular portion (Fig. 7A). The paranodular tissue was more normal in appearance (Fig. 7B) but it also showed an increased stroma due to edema.

COMMENT.—Thyroidectomy was performed 17 hours subsequent to giving the radioactive iodine. The nodule, which was colloid in character (Fig. 7A), but presented much varied evidence of degeneration, contained (Fig. 2 M. M.) 86.9 mg. per cent of elemental iodine, of which the diiodotyrosine fraction was largest, 63.6 mg. per cent, the thyroxine fraction being 17.8 mg. per cent and the inorganic fraction 1.9 mg. per cent. The paranodular tissue, which was more normal in appearance (Fig. 7B) and yet showed an increased stroma, clearly demonstrated a greater content of ordinary iodine (Fig. 2 M. M.), 190.2 mg. per cent, the diiodotyrosine fraction being largest, 144.8 mg. per cent, with the thyroxine 25.9 mg. per cent and the inorganic fraction 9.5 mg. per cent.

The nodule (Fig. 3 M. M.) also showed less avidity for radioiodine than the paranodular tissue, 14.0 per cent, and less production of physiologically active organic iodine, with the diiodotyrosine 11.4 per cent and the thyroxine fraction 2.1 per cent, the inorganic fraction being 0.35 per cent. The paranodular tissue, on the other hand (Fig. 3 M. M.), retained 90.0 per cent per 100 Gm. of dry gland of the radioiodine ingested, the diiodotyrosine fraction being largest, 82.8 per cent, with the inorganic 11.1 per cent and the thyroxine 6.7 per cent.

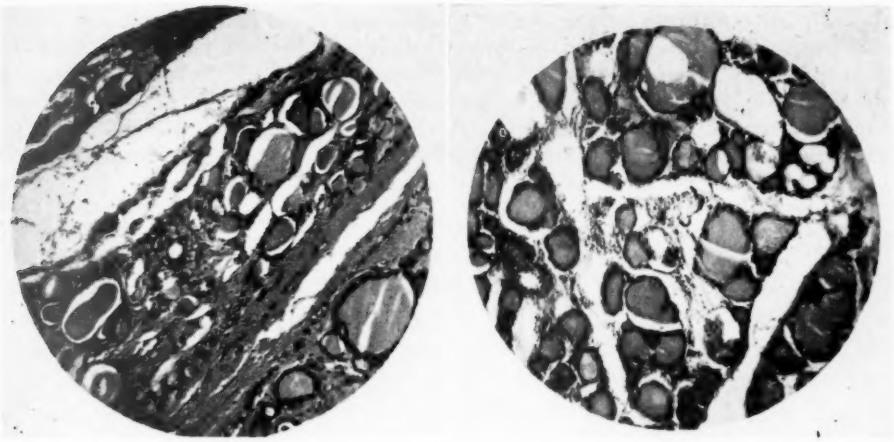
Protocol of R. G.—No. 445841, with Nodular Goiter with Mild Hypothyroidism: R. G., a white, married female, age 44, entered University Hospital, July 6, 1944, for management of nontoxic nodular goiter. She first became aware of adolescent goiter at 17 years of age, which subsequently almost disappeared. Later it enlarged during each of 12 pregnancies and receded during the intervals. It gradually enlarged five years ago and since then it has remained large. Only an occasional choking sensation accompanied its presence up to about two years ago when she began to be troubled with excessive weakness and easy fatigability. Loss of appetite was associated.

Physical examination showed a well-developed and well-nourished white female. Examination of the neck revealed a large nodular goiter.

Admission red blood count was 4,250,000, with the hemoglobin 12.5 Gm. per cent. The white blood count was 8,500, with the neutrophils 56 per cent, lymphocytes 42 per cent, and basophils 2 per cent. The urinalysis was negative. The average basal metabolic rate determination was minus 20 per cent, with the basal pulse 72, the respirations 10, the temperature 98°F., blood pressure 120/70, and the weight 141 pounds. The total blood iodine averaged 3.13 and the acetone-insoluble fraction 1.07 micrograms per cent, which are normal. The blood urea nitrogen was 18.0, and the blood sugar was 85 mg. per cent. The serum cholesterol was 250, with the free fraction 63, and the ester 185 mg. per cent (75 per cent). The blood prothrombin was 125 per cent of the average normal value, while the hippuric acid liver function test yielded 2.82 Gm., which is normal. The sedimentation rate was 17 mm. in one hour, which is normal. Roentgenography of the chest and neck revealed a left lateral deviation of the trachea.

Radioactive iodine was given in grape juice on July 24, 1944, about 40 hours before operation. Bilateral subtotal thyroidectomy was performed by one of us (I. D. P.) under avertin, cyclopropane, oxygen and helium anesthesia at 8:00 A.M. on July 26, 1944. The postoperative course remained generally uneventful.

The goiter as removed weighed 176 Gm. About 20 Gm. of thyroid tissue were left behind. The left lobe measured 11 x 3.5 x 5.5 cm. and the right lobe with the isthmus measured 11.5 x 3.5 x 6 cm. The goiter was grossly nodular and presented on cross-section many nodules of varying size, the smallest measuring 5 mm. and the largest 2.5 cm. in diameter. Most of the nodules were colloid in type and not completely circumscribed.

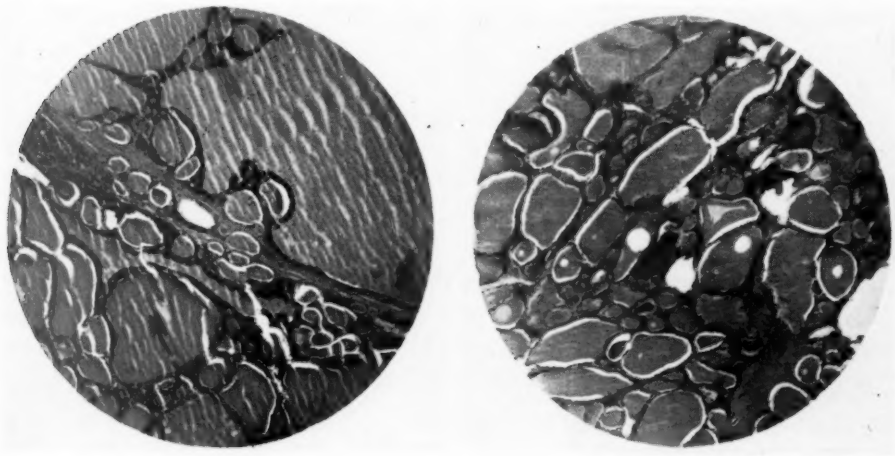


A B

FIG. 7.—Nontoxic Nodular Goiter.

(A) Nodule. Note the marked fibrosis, hyalinization and edema. The amount of acinar tissue is markedly decreased. (x 150)

(B) Paranodular tissue. This is more normal in appearance but shows stromal edema and a tendency to accumulation of colloid over normal. (x 150)



A B

FIG. 8.—Nontoxic Nodular Goiter.

(A) Colloid nodule. The nodule is typically colloid in character and shows formation of follicles of enormous size filled with much colloid. There are also areas of hyperplasia with plication. (x 150)

(B) Paranodular tissue. This tissue shows stromal fibrosis and hyalinization with a tendency to increased colloid accumulation suggestive of colloid goiter. (x 150)

Grossly, these appeared much like the surrounding tissue. Evidences of fibrosis, fatty degeneration and old hemorrhage were present. Nodular tissue was moderate in amount while the paranodular tissue was abundant and practically all located in the upper pole and posterior areas. The paranodular tissue also showed moderate fibrosis. Microscopically (Fig. 8), the nodular and paranodular tissue studied showed similar degenerative changes and differed in that the nodule was typically colloid in character and showed a greater tendency to formation of follicles of enormous size with flattened epithelium and filled with much colloid, as well as few areas of hyperplasia. *Final Surgical Diagnosis:* Nontoxic nodular goiter.

COMMENT.—This patient was thyroidectomized about 40 hours subsequent to administration of radioiodine, the interval being about twice as long as for other patients investigated. The nodular tissue (Fig. 2 R. G.) contained 66.0 mg. per cent of the ordinary iodine I^{127}, of which 51.0 mg. per cent were distributed in the diiodotyrosine fraction, 9.2 mg. per cent in the thyroxine, and 2.4 mg. per cent in the inorganic fraction. The paranodular tissue (Fig. 2 R. G.) showed a definite increase in the retention of iodine over the nodular tissue. It contained 113.0 mg. per cent of iodine per 100 Gm. of the dry gland, of which the diiodotyrosine fraction was largest, 80.0 mg. per cent, the thyroxine fraction being 20.5 mg. per cent, and the inorganic fraction 2.6 mg. per cent.

Study of this goiter showed slightly less avidity for radioiodine by the nodular than by the paranodular tissue (Fig 3 R. G.). Except for less avidity for iodine, the paranodular tissue simulated, to a greater extent, the fractional distribution of iodine in the nontoxic diffuse colloid goitrous tissue of M. H. and E. S. The nodular tissue stored 103.0 per cent per 100 Gm. of the dry gland of the radioiodine given 40 hours before thyroidectomy, of which 95.0 per cent were distributed in the diiodotyrosine fraction, 3.8 per cent in the thyroxine, and 3.6 per cent in the inorganic fraction. The paranodular tissue contained 124.0 per cent per 100 Gm. of the dry gland, of which 106.0 per cent was distributed in the diiodotyrosine fraction, 59 per cent in the thyroxine, and 4.6 per cent in the inorganic fraction.

It is not surprising that there is the least percentage difference in the avidity and fractional distribution of radioiodine between the nodular and paranodular tissue of this gland (Fig. 3 R. G.) when compared to other nodular goiters studied. As mentioned above, the nodules were colloid in type, appeared much like the surrounding tissue, and grossly were not completely separated from the paranodular tissue. Microscopically, the nodular (Fig. 8A) and paranodular (Fig. 8B) tissue studied also showed almost similar degenerative changes and differed only in that the nodule was typically colloid in character and showed more tendency to formation of follicles of enormous size as well as a few areas of hyperplasia.

Note also that the content of ordinary iodine is less and that the avidity for radioiodine by both the nodular and paranodular tissues of this goiter is greater than that of nontoxic nodular goiters of the other patients, which may indicate that the hypothyroidism here is due to an iodine deficiency. On the

other hand, the increase in storage of radioactive iodine may have been due to the longer interval between radioiodine administration and thyroidectomy.

Protocol of L. D.—No. 445388, with Mildly Toxic Nodular Goiter: L. D., a colored maid, age 56, was admitted to University Hospital on April 3, 1944, for surgical treatment of goiter.

She had had a goiter since the age of 16 years. This remained symptomless until recent years. About four years ago she experienced sweating, generalized nervousness, restlessness, palpitation and dyspnea. Severe headaches and occasional nausea and vomiting were associated. Loss of weight from 190 to 173 pounds had occurred during the past three weeks. She was a known diabetic for nine years, this being controlled by diet and insulin. Supravaginal hysterectomy had been performed in 1916.

Physical examination showed an obese colored female lying quietly in bed. A slightly nodular, moderately large bilateral goiter was palpable. The right was the larger.

Admission red blood count was 4,260,000, with the hemoglobin 16 Gm. per cent. The white blood count was 5,740, with the neutrophils 46 per cent, lymphocytes 41 per cent, monocytes 9 per cent and eosinophils 4 per cent. The urinalysis was negative. The blood Wassermann and Mazzini tests for syphilis were negative. The basal metabolic rate on April 4, 1944, was plus 17 per cent, with the basal pulse 88, respirations 17, temperature 98.2°F., blood pressure 172/100, and the weight 173 pounds. The total blood iodine was 4.82 on April 4, 1944, with the acetone-insoluble fraction 2.20 micrograms per cent. The blood urea nitrogen was 10, and blood sugar 121 mg. per cent. Phenolsulfonphthalein test of renal function showed 60 per cent excretion during the first hour and 5 per cent excretion during the second hour after intravenous injection. Blood cholesterol was 75.0 mg. per cent, which is low. Divided 24-hour urine specimens showed no sugar. Prothrombin was 57 per cent, which is low, and increased to 98 per cent after intramuscular synkayvite. Hippuric acid test of liver function was 2.5 Gm. per cent.

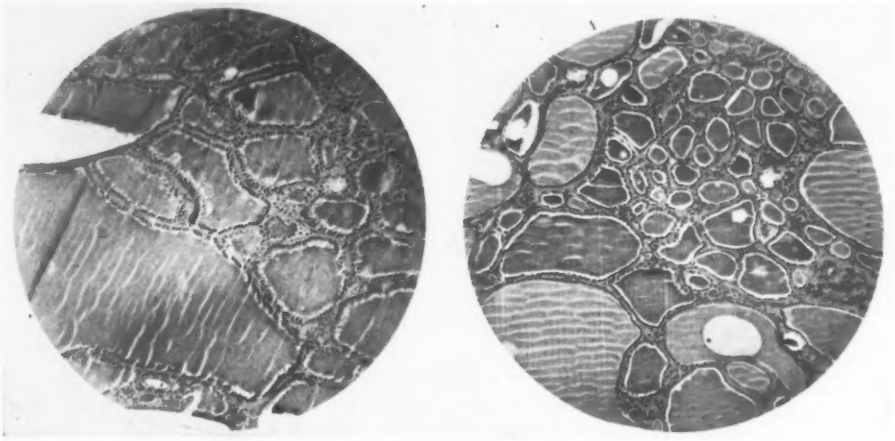
Because the patient developed an upper respiratory infection with acutely inflamed nasal and oropharyngeal mucosae, operation was postponed. She reëntered University Hospital on June 23, 1944. During the interval the upper respiratory infection subsided. Preoperative therapy included rest, sedation, adequate control of the diabetes and a high calcium, phosphorus and vitamin intake. Iodine had been given up to May 25, 1944. The basal metabolic rate was plus 18 per cent on June 24, 1944, with the basal pulse 88, respirations 17, temperature 98.2°F., blood pressure 152/92, and the weight 172 pounds. The blood sugar was 157 mg. per cent. Divided 24-hour urine specimens showed practically no urinary sugar excretion.

Radioiodine was given orally in grape juice at 12:45 P.M. on June 25, 1944. Subtotal thyroidectomy was performed by one of us (I. D. P.) under avertin, cyclopropane, oxygen and helium anesthesia on June 26, 1944, at 11:45 A.M. During the postoperative course the diabetic status was carefully followed and the postoperative reaction remained minimal. She made an uneventful recovery. The diabetes, subsequently, could easily be controlled by diet, without insulin.

The goiter, as removed, weighed 118 Gm. It contained a moderate amount of nodular tissue. About 15 Gm. of fairly normal-appearing thyroid tissue were left behind. The right lobe measured 9 x 5 x 2.5 cm. It contained numerous nodules of varying size, the largest measuring 2 cm. in diameter. There was also present a considerable amount of paranodular thyroid tissue containing a moderate amount of colloid. The nodules were colloid in character and definitely circumscribed. Various degenerative changes including fibrosis, old hemorrhage and small cyst formations were present to a slight extent. The amount of paranodular definitely exceeded the nodular tissue. The left lobe measured 10.5 x 5 x 2.5 cm. and showed pathologic changes quite similar to the right lobe but contained much more diffuse paranodular colloid tissue and fewer colloid nodules. The isthmus measured 6 x 3.5 x 2 cm. Its appearance on cross-section was that of the left lobe. It contained one calcified nodule. Microscopically, the nodule studied (Fig. 9A) was

typically colloid in type. The mild hyperplasia, increase in height of the epithelial cells and the marked vacuolation are believed by some pathologists to represent considerable hyperactivity. The paranodular tissue (Fig. 9B) showed areas of involution.

COMMENT.—There was a delay of 23 hours between radioiodine administration and thyroidectomy. The nodules were definitely circumscribed by fibrous connective tissue which may explain the lower content (Fig. 2 L. D.), of elemental iodine I^{127}, 77.0 mg. per cent, of the nodular than of the paranodular tissue, 180.2 mg. per cent. Diiodotyrosine constituted the largest nodular iodine fraction, 63.2 mg. per cent, the thyroxine iodine being 10.0 mg. per cent and the inorganic fraction 1.0 mg. per cent. The paranodular elemental iodine fractions consisted of 108.2 mg. per cent diiodotyrosine, with thyroxine 63.3 mg. per cent and the inorganic fraction 3.5 mg. per cent.



A B

FIG. 9.—Toxic Nodular Goiter.

(A) Typical colloid nodule (x 150). The mild hyperplasia, the increase in height of the epithelial cells and the marked vacuolation are said to indicate considerable activity.

(B) Paranodular tissue. (x 150). This tissue is more normal in appearance but also shows flattened epithelium and large follicle formation suggestive of colloid goiter.

The nodule also developed an avidity for radioiodine (Fig. 3 L. D.) of 16.5 per cent, which is much less than the 92.1 per cent of the paranodular tissue (Fig. 3 L. D.). The nodular diiodotyrosine iodine was 11.0 per cent, with the inorganic fraction 3.0 per cent and the thyroxine iodine 2.1 per cent. On the other hand, the paranodular tissue (Fig. 3 L. D.) showed remarkable production of 50.9 per cent of thyroxine iodine which is much greater than the 2.1 per cent of the nodular tissue and the 8.5 per cent of the paranodular tissue of the nontoxic goiters. This would indicate that the paranodular tissue is here responsible for the hyperthyroidism. The diiodotyrosine radioiodine was 15.8 per cent and the inorganic fraction 7.6 per cent.

DISCUSSION.—A surgicopathologic study was made of the nodules of six patients with various clinical types of thyroid disease and varying degrees of

toxicity. This study showed wide variations in their histologic picture from a colloid nodule, which is highly differentiated, to a true fetal adenoma, with little degree of differentiation. The nodules of the patients with toxic nodular and exophthalmic goiter were of the hyperplasia-involution type and not so-called true adenoma in type. Even though the nodules varied greatly microscopically, it is significant that the intensity of their activity was quite independent of the gland function. The nodules produced considerably less amounts of physiologically-active organic iodine compounds than the surrounding thyroid tissues, as indicated by the ordinary iodine I^{127} (Fig. 10) and radioiodine I^{131}

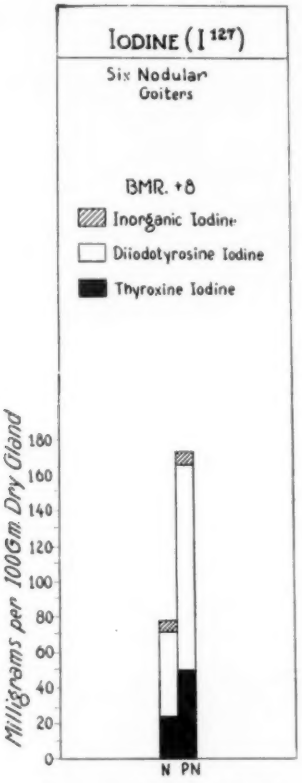


FIG. 10.—N—Nodular thyroid tissue, PN—Paranodular thyroid tissue.

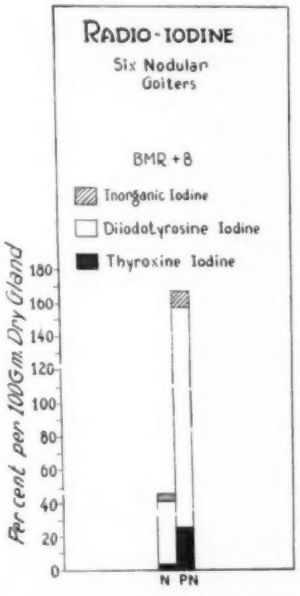


FIG. 11.—N—Nodular thyroid tissue, PN—Paranodular thyroid tissue.

(Fig. 11) fractionation studies.[17] The ordinary iodine data confirms the work of Marine.[14] None of the nodules studied could be considered so-called hyperfunctioning adenomas. These studies also indicated that some nodules, such as the fetal adenoma, contributed very little to the total thyroid function.

The nodules of the patients with toxic nodular and exophthalmic goiter studied also appeared functionally autonomous, since much less thyroid hormone was made by them than by the surrounding thyroid tissue. In the two hyperthyroid patients studied, the thyroxine-making activity was 7 and 25

times greater in the paranodular tissue over that of the corresponding nodules. The diiodotyrosine- and thyroxine-making activity of the nodules of the toxic nodular goiter patient appeared no different than that of the nodules of the nontoxic nodular goiter patients. One of the three small nodules of the exophthalmic goiter patient was studied and showed a slightly increased activity over that of the nodules of nodular goiter. This evidence suggests that the hyperactivity of the thyroid gland of the patients studied with toxic goiter does not arise from the nodules and that they are functionally incidental lesions.

The diffuse colloid tissue of two nontoxic goiters (M. H. and E. S.) revealed an increased avidity for radioiodine which exceeded that of the patient with toxic nodular goiter and approached that of the diffuse hyperplastic tissue of exophthalmic goiter (R. D.). However, the thyroxine-producing activity of the paranodular thyroid tissue of the patients with toxic nodular goiter and with exophthalmic goiter greatly exceeded the thyroxine-producing activity of all other forms of nontoxic pathologic thyroid tissue studied. It was 4.5 times greater than the thyroxine-producing activity of the diffuse colloid tissue and 5 times greater than that of its own nodules. It averaged 29 times greater than the activity of the nodular tissue and 7.5 times greater than the thyroxine-making activity of the paranodular tissue of three patients with nontoxic nodular goiter. The paranodular tissue showed least thyroxine-making activity in a patient (R. G.) with nodular goiter and hypothyroidism.

In previous studies[21, 22] we pointed out that in exophthalmic goiter, even in the presence of continued excessive loss of iodine and a decreased content of thyroid iodine, the diffuse hyperplastic thyroid gland retained a greater than normal avidity for this element. Radioactive iodine studies again emphasize the great avidity for iodine shown by the diffuse hyperplastic gland of Graves' disease and also point out that the ability of the gland for thyroxine and diiodotyrosine formation is greatly increased. This signifies that the factor of thyroid constipation or increased storage of the thyroid hormone in the thyroid follicle is the probable cause of the beneficial effects of iodine therapy in hyperthyroidism.

We have often wondered why surgeons can even remove several hundred grams of adenomatous tissue from the patient with nontoxic nodular goiter, leaving behind only a few grams of the diffuse paranodular tissue and still without producing an appreciable change in the thyroid function or in the basal rate of metabolism. Why is it that similar large amounts of adenomatous tissue can be removed from the patient with toxic nodular goiter without producing postoperative hypothyroidism? These studies indicate that often the adenomatous tissue contributes little to the total thyroid function which no doubt explains the good surgical therapeutic end-results obtained in the usual case of toxic or nontoxic nodular goiter.

Our small series of cases indicates that the surgeon doing nodular goiter surgery should also be concerned with the amount of paranodular tissue to preserve. This, in order to save the optimum thyroid function for the patient. The diffuse paranodular tissue of all cases of nodular goiter (Figs. 1B, 6B, 7B, 8B and 9B) studied, presented many of the microscopic characteristics of

diffuse colloid goiter. The diffuse paranodular tissue of nontoxic nodular goiter and of nodular goiter with hypothyroidism acted biochemically to a greater extent, like the tissue of nontoxic diffuse colloid goiter (Figs. 12 and 13), which suggests that during thyroidectomy it is this tissue which should be conserved to protect the patient against further decrease in the function of the thyroid gland. Iodine, as well as desiccated thyroid when needed, should be given the patient postoperatively to help restore the remaining tissue to as normal as possible, for the same reason that iodine is given to the patient with adolescent goiter. On the other hand, in nodular goiter with hyperthyroidism the paranodular tissue acted biochemically to a greater extent, like the tissue of exophthalmic goiter (Figs. 12 and 13) and this tissue should be adequately resected to decrease the incidence of persistence or pseudorecurrence of the hyperthyroidism.

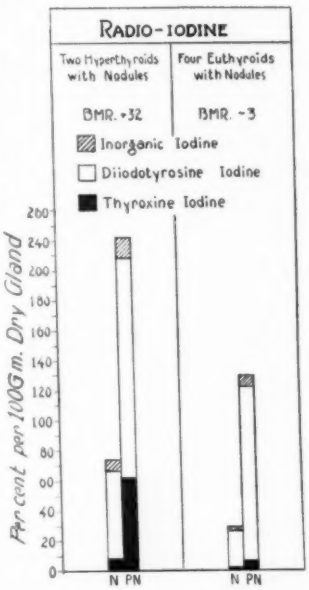


FIG. 12.—N—Nodular thyroid tissue, PN — Paranodular thyroid tissue.

Fortunately, in our experience, it frequently happens that the upper and posterior portions of the nodular gland (Figs. 14 and 15) are less affected by the degenerative processes, so that most of the paranodular tissue is located in this area and a reasonable margin of tissue free from adenomatous and cystic areas may be preserved in nontoxic nodular goiter (Fig. 16). It is almost invariably possible, also, to save a portion of the lower pole since this area does not share as often in the degenerative processes to the same extent as the lateral and anterior portions of the lobe. On the other hand, since the paranodular tissue is frequently similarly located near the danger zone (Figs. 14 and 15) even in patients with severe toxic nodular goiter when a more complete resection is indicated, the thyroidectomy must then be performed with added precaution. But by judicious planning of the plane of resection a large part of each lobe of the thyroid of the toxic nodular goiter patient can be excised (Fig. 16), when indicated, including especially the paranodular tissue and only fragments of thyroid tissue along with the recurrent laryngeal nerves and the parathyroid glands can be preserved at the sites already named.

The number of cases are too few to make far reaching conclusions and the data available at this time permit only a preliminary summary. They do indicate strongly that further studies in this direction should prove valuable. None of the patients who received tracer doses of radioiodine developed deleterious effects. All were followed carefully postoperatively for about one year and none developed evidences of hypometabolism. The basal metabolic rates on discharge from the Thyroid Clinic varied from minus 11 to plus 8 per cent, and all showed clinically a normal thyroid function.

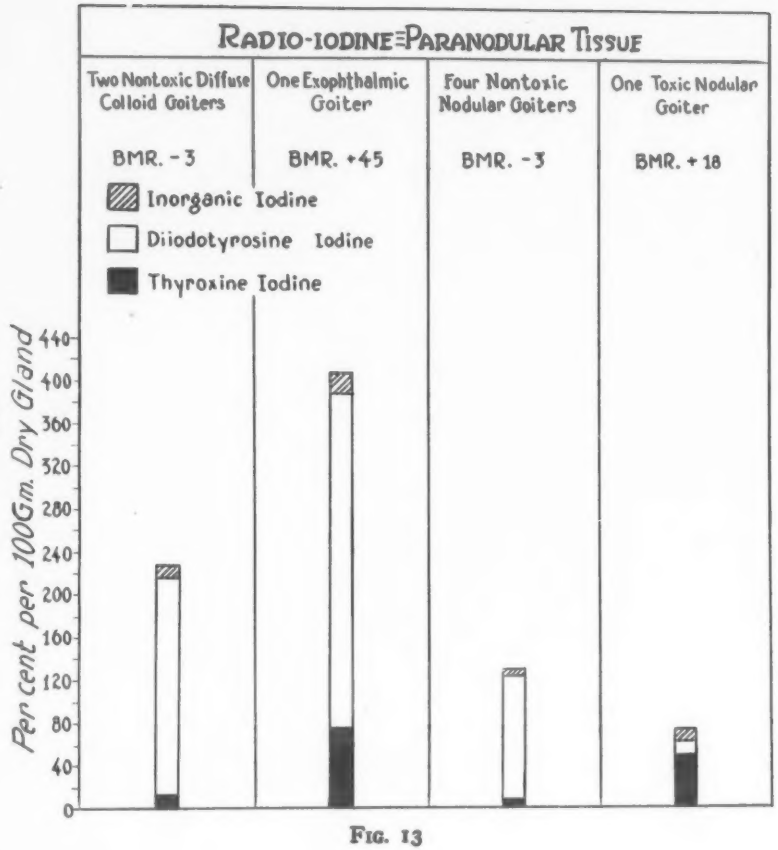


FIG. 13

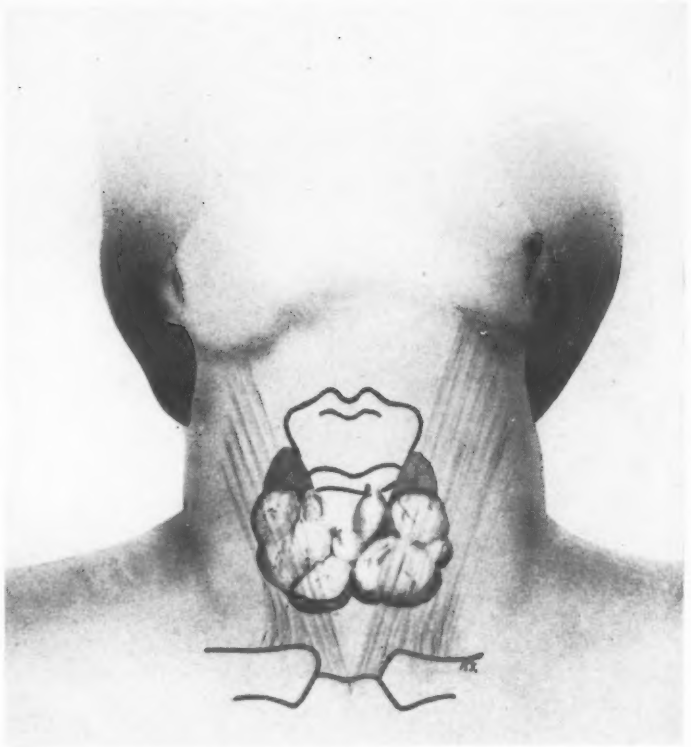


FIG. 14.—Frequently the paranodular thyroid tissue (shaded) is located to a great extent in the upper pole area. The lower pole area may not share in nodulation.

FIG. 15.—The posteromedial portion (shaded and demarcated by an interrupted line from the nodular goitrous tissue) of the thyroid gland not infrequently remains free of nodulation.

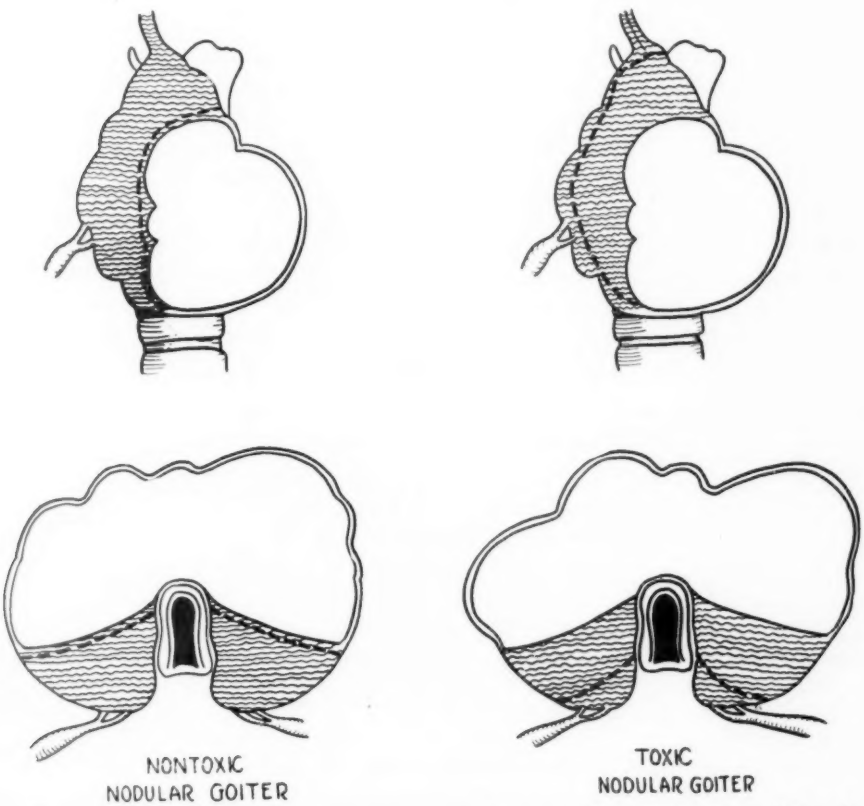


FIG. 16.—In nodular goiter surgery as much as possible of the paranodular tissue (shaded) should be conserved for the patient with nontoxic nodular goiter. The goitrous tissue should be more radically removed from the patient with toxic nodular goiter.

SUMMARY AND CONCLUSIONS

(1) Radioactive iodine and ordinary iodine fractionation as well as surgicopathologic studies were made of seven patients with various clinical types of thyroid disease and varying degrees of toxicity. The histologic pictures of the nodules of the six patients who had nodular goiter showed wide variations. The nodules of the patients with toxic nodular and exophthalmic goiter were of the hyperplasia-involution type and not so-called true adenoma in type. All nodules showed a decreased function when compared to the function of the corresponding paranodular thyroid tissues. The nodules of patients with nontoxic nodular goiter, toxic nodular goiter, exophthalmic goiter, and so-called fetal adenoma studied appeared functionally autonomous. They showed less avidity for administered radioiodine, and also much less thyroxine and diiodotyrosine was made by them than by the surrounding thyroid tissue.

(2) The diffuse goitrous tissue of two patients with nontoxic diffuse colloid goiter showed great avidity for iodine but its ability to produce thyroxine and diiodotyrosine did not appear greatly increased.

(3) The diffuse hyperplastic tissue of a patient with exophthalmic goiter showed the greatest avidity for iodine and the greatest ability to produce thyroxine and diiodotyrosine.

(4) The diffuse paranodular thyroid tissue of three patients with nontoxic nodular goiter, one having a mild hypothyroidism, showed many of the microscopic characteristics of diffuse colloid goiter. It acted biochemically to a greater extent like the tissue of nontoxic diffuse colloid goiter, which indicates that during thyroidectomy it is this tissue which should be left behind to protect the patient against further decrease in the function of the thyroid gland. Iodine should perhaps be given postoperatively to help restore the remaining tissue to as normal as possible.

(5) The paranodular thyroid tissue of a patient with toxic nodular goiter acted biochemically to a greater extent like the diffuse hyperplastic tissue of exophthalmic goiter, which suggested that this tissue should be more adequately resected to decrease the incidence of persistence or pseudorecurrence of symptoms.

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MALIGNANT ADENOMA OF THE THYROID, WITH SECONDARY METASTASES TO BONE

WITH A DISCUSSION OF SO-CALLED "BENIGN METASTASIZING GOITER"

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DURING the past 20 years on the Public Wards of the Toronto General Hospital there have been performed a total of 2,268 thyroidectomies. Sixty of these thyroidectomies, or 2.6 per cent, were done for carcinoma of the thyroid. Of these 60 cases, 24 were diagnosed as adenocarcinoma or malignant adenoma of the thyroid. Five of these cases of malignant adenoma had metastases to bone.

I should like to limit the scope of this paper to a discussion of the five cases from this group of malignant adenomata, with secondary bony metastases, which were similar to each other in that not only did their symptomatology first direct attention to the secondary tumor, but biopsy of this tumor showed that it was made up histologically, in part, or completely, of apparently quite benign thyroid tissue.

The first case was admitted because of a mass involving the right zygoma, which was made up for the most part of benign thyroid tissue, although portions of the tissue were atypical enough to suggest its malignant nature.

Case 2 presented herself because of a tumor of the parietal bone, which on section proved to be benign thyroid tissue.

Case 3 was sent in because of a destructive tumor of the radius. No signs or symptoms suggested the thyroid gland as the offender until biopsy report was returned as benign thyroid tissue.

Case 4 came in because of a paraplegia of gradual onset involving her lower limbs. Biopsy of a tumor of the 5th thoracic vertebra revealed benign thyroid tissue.

In Case 5, the general pattern differs from the others in that she had a thyroidectomy, because of pressure symptoms, and malignant adenoma removed, only to develop paraplegia from a metastasis in the cervical spine seven weeks later. This was removed, and following roentgenray treatments she has apparently made a complete recovery.

This interesting condition was first described by Cohnheim,[1] in 1876, and called by him "benign metastasizing goiter." That it was possible for a benign tissue to break off cells into the blood stream and form distant metastases of similarly benign tissue, is so contrary to the accepted laws governing histopathology, as to have continued to intrigue the clinician as well as the pathologist since that time. In comparatively recent years, evidence seems to be accumulating to suggest that in spite of their benign appearance, these tumors are actually malignant.

Historically, Cohnheim's original case is of interest because it has been

frequently quoted in the literature to support the theory of the possibility of benign metastases.

A woman, age 35, developed multiple small gelatinous metastases in bronchial nodes, lung, femur and lumbar spine. The thyroid gland was diffusely and symmetrically enlarged, and contained two nodules similar in gross and microscopic appearance to the metastatic seedlings. One of these nodules showed invasion into the lumen of the left inferior thyroid vein. Histologic appearance of the thyroid nodule was that of simple colloid goiter and the metastases revealed a similar cellular structure except that a few small acini contained no colloid and some of the follicles showed the presence of epithelial nests.

Cohnheim concluded that this was a case of simple colloid goiter, with metastases. He skipped lightly over the fact of the invasion of the lumen of the left inferior thyroid vein, saying that it had been noted before in cases with no metastases. He attempted to explain the presence or absence of metastases in these cases of venous invasion by assuming a special constitutional individuality which made metastases possible in some and not in others. Thus, in this original case, the presence of (1) metastases; (2) venous infiltration; and (3) epithelial cell nests make its benign nature, in the light of our present knowledge, highly problematical.

In 1899, Honsell[2] made a spirited defense of Cohnheim's conclusions. He discussed at some length the possibility of the benign thyroid metastases being displaced thyroid anlagen. Considerable work has been done on this subject and it has become firmly established that although aberrant thyroid tissue is a fairly common anomaly, it is found in places close to the site of its primitive origin. Aberrant masses, derivatives of the thyroglossal duct, may be found in the midline almost anywhere from the foramen caecum in the tongue to the arch of the aorta. Lateral aberrant masses, remnants from the branchial cleft derivatives are found usually about the middle of a line joining the midclavicle to the mastoid. In these positions aberrant thyroid gland tissue is commonly found, and is not infrequently associated with carcinomatous changes.

The one exception to this rule of thyroid tissue arrests being found in the neighborhood of the gland origin is in the case of teratomata which are occasionally encountered chiefly in ovaries, testes and the sacral area. This tumor occasionally contains mature thyroid tissue together with the other tissues which go to make up its complex structure.

Bearing these facts in mind, the theory that normal thyroid tissue may develop from developmental cell arrests in scattered foci throughout the body becomes highly unlikely.

In 1926, Simpson[3] reported three cases of so-called "benign metastasizing goiter," all of whom died within three years of frank carcinoma of the thyroid gland. In the same paper he reviewed in detail 77 cases reported in the literature of this condition. These were all the cases he could find. He found that the diagnosis in nearly every case was made on the benign microscopic appear-

ance of the secondary tumor and the presence of a clinically benign thyroid gland. Of the 77 cases, a microscopic examination was made in but 29 cases and an autopsy in only 33. Several of the cases hastily reported following pathologic examination of the biopsy from the metastases, were later reported as having died from undoubted carcinoma of the thyroid. He concluded that these cases had been inadequately studied and that existence of the possibility of their being such a thing as benign thyroid tissue seeding the body with innocent metastases was highly unlikely. In recent years it has become generally accepted that in spite of their innocuous appearance, these metastases are actually malignant and are always derived from a primary carcinoma, usually a malignant adenoma, of the thyroid gland.

A malignant adenoma is thought to arise from a fetal adenoma. They vary greatly in size and appearance. They may become large and exert their malignant effect mainly by pressure in the neck or they may remain very small and give rise to metastases which terminate life. They differ chiefly from genuine carcinoma in being encapsulated and being considerably slower in their rate of growth.

The microscopic appearance of the malignant adenoma varies greatly, both in different specimens and in different parts of the same specimen. Most often the appearance is that of cubical or low columnar cells arranged in acini which frequently contain colloid material—while in places the cells may be disposed in solid masses or even present a papillary type of formation. In the same tumor there may be portions resembling normal hypoplastic thyroid tissue in one area, solid carcinomatous masses in another, or papillary adenocarcinoma in yet another.

According to Ewing,[4] in the metastases from this type of tumor "the microscopic structure is usually of a more adult type than the original tumor and many of the acini appear as fully-developed normal thyroid acini containing colloid. The metastases, however, may differ in their microscopic appearance just as the original primary in the thyroid differs in different parts of the tumor, thus, giving rise to the so-called "benign metastases" and "malignant metastases" depending on the histologic appearance of the metastatic nodule. The character of the tissue found within the metastatic nodule corresponds always in morphology to some portion of the original tumor, though it is not always possible to demonstrate the histologic criteria of malignancy in it."

Graham[5] concluded from his studies that the morphologic characteristics of the cells and tissue structure was an unreliable method of determining the the presence of malignancy. He felt that in his series that only 30–40 per cent of malignant epithelial tumors of the thyroid could be diagnosed by the histologic appearance alone. The most constant single indication of epithelial malignancy was the invasion of blood vessels. It is probable that metastases from these tumors originate at such a site and travel to their proliferative focus *via* the blood stream.

Reinhoff[7] makes the statement that "there is an inherent tendency on the part of thyroid cells that have passed into the blood stream or lymph circula-

tion, after becoming lodged in an organ or tissue, to develop into normal thyroid tissue, so that, after metastasizing, an original carcinomatous area may appear benign. Metastases from normal thyroid do not occur."

CASE REPORTS

Case 1.—(A25011): A. R., male, age 42, of Scottish descent, carpenter, was first admitted in February, 1937, with a history that 18 months earlier he first noticed a small lump just in front of his right ear. It was about the size of an olive, hard, painless, and, at the onset, associated with some stiffness of the right side of the neck. A month later he noticed increasing fatigue which symptom together with a loss of 25 pounds persisted until his admission. The lump gradually increased in size.

Upon admission to hospital, he had a large pulsatile swelling the size of half an egg over the right zygoma and a similar mass involving the 5th rib in the anterior

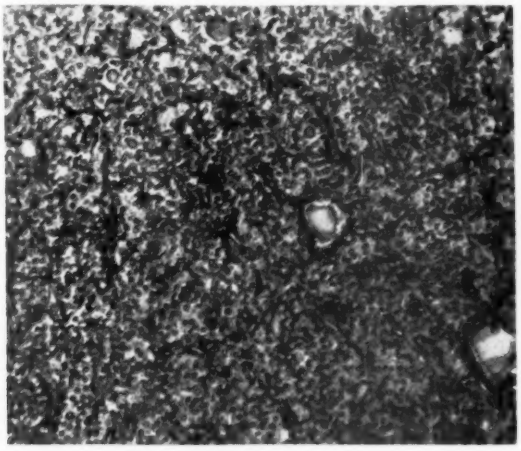


FIG. 1.—Case 1: S-37/472. Secondary metastasis showing tendency of cells to form cords.

axillary line and a third pulsating mass over 2L vertebra. A small hard nodule the size of a bean was felt in the right lobe of the thyroid. There was nothing of significance on blood examination. His Wassermann was negative. B. M. R. was +37. There was no definite sign or symptom suggestive of hyperthyroidism.

Biopsy (S—37/472) taken from the tumor of the right zygoma revealed an extremely cellular mass, sections of which reproduced fairly typical thyroid gland acini. These acini were well filled with colloid material. Other sections showed cuboidal cells growing in small compact pseudo-acinar arrangements and in cylindrical cords (Fig. 1). In several areas invasion of blood vessels was noted and its malignancy was further demonstrated by the atypical characteristics of the individual cells, their lack of polarity, abundant mitotic figures as well as the inability of the tissue to accurately reproduce thyroid tissue throughout.

A partial thyroidectomy was then performed and the right lobe containing two adenomata removed but the left which felt quite normal was not touched. At the time of operation it was noted that the gland was easily freed, with no evidence of invasion beyond the capsule of the adenoma.

Section of the right thyroid lobe (S—37/893) revealed a normal gland except for these two adenomata made up of the same malignant composition as their metastases. A re-check B. M. R. shortly after his thyroidectomy was +45.

This man was then referred to the Radiologic Department for treatment of his secondaries with deep roentgen therapy which began in March, 1937.

Roentgenologic examination, December 17, 1937, revealed further secondaries in L1 and L4, left pubic and right wing of ilium.

February 3, 1939, it was noted that the lesion on the right temporal area had diminished somewhat in size and had become softer as a result of high voltage therapy. However, it had not disappeared and, as its reaction to treatments was being used as a therapeutic test of radio sensitivity, the conclusion was drawn that these metastases were fairly resistant to the roentgenray.

He was again admitted in June, 1939, because of a large metastasis involving his left femur. He was fitted with a walking caliper on this admission. Examination on this second occasion revealed the fact that although the roentgenray treatments had helped to partially relieve his pain it was unable to check the growth of the secondary tumors.

He developed a spastic paraplegia and cord bladder in August, 1939, and died in June, 1940, just five years after the onset of his trouble.

Postmortem Examination.—(No. 1241): The site of the primary tumor was represented by a small amount of partially fibrosed thyroid tissue. The metastases, which were composed for the most part of fairly typical thyroid acini, were confined entirely to the osseous system. They were discreet and growth had occurred almost entirely in an expansile manner with very little tendency toward invasion of the surrounding tissues. There was a large circumscribed tumor of the right zygoma and temporal bone which had destroyed the bony plate of the skull and, by expansion beneath the dura, had compressed the underlying temporal lobe. Similar circumscribed tumors were attached to both the 5th rib and the right ischium and there were extensive deposits in the vertebrae, with two pathologic fractures. Compression of the cord by tumor in the midthoracic region accounted for the patient's paraplegia. The left femur at the junction of the middle and upper thirds showed partial destruction by tumor.

Case 2.—(A28225): Mrs. A. S., female, age 73. This patient was first treated in this hospital in April, 1937, at which time she had a spinal cord tumor removed from the level of the 1st thoracic vertebra. This tumor on pathologic examination proved to be a meningioma.

In October, 1945, she was again admitted—this time because of a tumor of the skull. She stated that eight months previously, she had fallen and bumped her head and two weeks later noticed a swelling of the left parietal region. This has been increasing slightly in size but gave her no trouble. On admission, it was noted that she had a firm, painless nodule the size of a walnut in the left parietal region which lay deep to the skin and was attached to bone. A roentgenogram showed a punched-out decalcified area about 1.5 inches in diameter. Her thyroid gland contained two small, firm, painless nodules.

The tumor of the skull was removed (S—5711/45) together with a surrounding block of bone, of both the inner and outer tables which had been erroded through. There was no evidence of invasion of scalp or dura. Because of her age it was felt unwise to do more than remove the secondary tumor locally.

Pathologic examination revealed a reddish hemorrhagic appearance of the tumor on cut-section. It contained multiple cystic spaces of varying sizes some of which contained colloid.

The microscopic examination revealed typical benign thyroid tissue.

The thyroid alveoli were well-formed. They were lined by a single layer of cuboidal-to-columnar epithelial cells. Their lumen contained colloid. There was no evidence of malignancy of this thyroid metastasis. There was no evidence of infiltration of tumor cells into the surrounding bone or the scalp tissues overlying the outer table.

Case 3.—(B82194): Mrs. V. S., female, Polish, age 41, housewife. Admitted February 28, 1946, with a history of occasional pain down the right forearm and wrist for three years, noticed chiefly on movements of supination, such as wringing out the

clothes. Pain, however, has never been a marked feature of her story. One and one-half years ago she struck her right forearm, following which she noticed the gradual development of a lump.

On admission, there was a firm, pulsating, slightly tender mass, the size of an orange, involving the upper and outer aspect of the right forearm.

Roentgenograms showed the tumor to involve the upper one-quarter of the right radius, with the exception of the head and 0.5 inch of neck. There was complete destruction of the shaft of the bone, the destructive process beginning abruptly from apparently normal bone at each end. A fine network of radiopaque threads ran through the mass, the picture suggesting a mass of soap bubbles (Fig. 2). The roentgenograms suggested benign giant cell tumor or possibly an osteolytic sarcoma. Roentgenograms of the remaining osseous system failed to disclose other tumor masses.

FIG. 2.—Case 3: (262158) Roentgenographic appearance of secondary tumor of the radius.

It was not until a biopsy (S—46/1266) was done that the true nature of the condition became apparent. The section consisted of connected cords of acidophilic cells grouped in alveolar formation and containing colloid (Fig. 3)—a typical picture of benign metastasizing tissue.

There was nothing to suggest, in the history or the examination, the possibility of hyperthyroidism. B. M. R. was +8. Two very small nodules were palpable in the right lobe of the thyroid.

A subtotal thyroidectomy was performed March 22, 1946, at which time two adenomatous masses were found, one benign and the other malignant (S—46/1662). The malignant adenoma was made up mostly of fairly typical thyroid cells lying in cords or in irregular masses within a thick capsule (Fig. 4). In the adjacent tissue were found veins completely filled with parenchymal cells similar to those of the adenoma (Fig. 5).

March 31, 1946, the tumor of the radius was resected together with the normal-appearing head at one end and part of the shaft at the other. The tumor was soft, encapsulated and contained filmy shells of bone which broke under the examining fingers like fresh corn flakes.

Following operation her B. M. R. was +4.

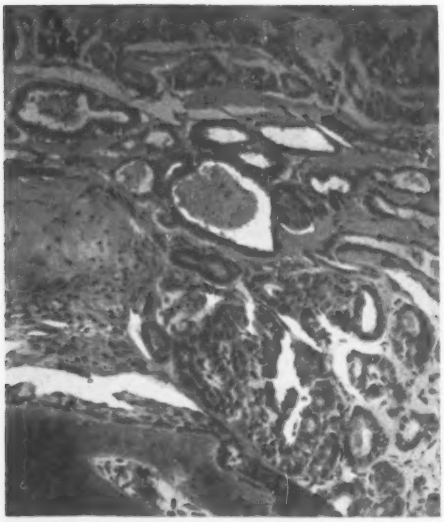
Case 4.—(B67357): Mrs. B. B., female, age 67, housewife. Following a fall two years ago this patient noticed the gradual onset of weakness and numbness in both legs. When first admitted, in March, 1945, she had complete loss of motor power of both legs, and loss of pain, touch and vibration sense below the xiphisternum level. There was urinary retention. Blood Wassermann was negative.

Roentgenograms revealed a tumor, thought to be an hemangioma, involving the 5th thoracic vertebra and the proximal portion of the posterior end of the 5th left rib.

Laminectomy was performed in April, 1945, and a very vascular tumor removed. Microscopic examination (S—45/1943) revealed thyroid tissue which, on the whole, was benign in appearance but in portions showed the presence of mitotic figures and a heaping-up of epithelial elements. There was a definite infiltration of the ligamentum subflavum.

The right lobe of the thyroid was enlarged. This enlargement had been present since adolescence though was possibly somewhat larger at present.

FIG. 3



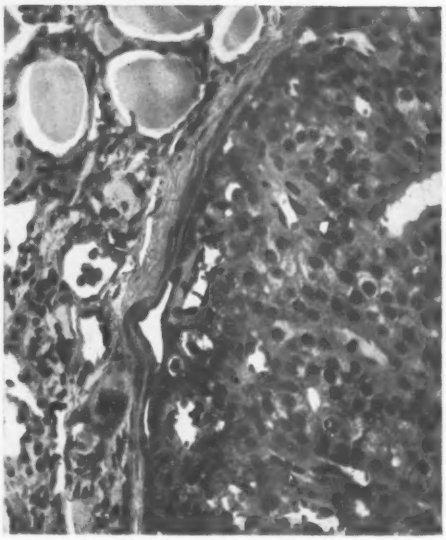


FIG. 4 FIG. 5

FIG. 3.—Case 3: (S—46/1266) Secondary metastatic tumor. In one corner is a fragment of bone of the radius. The remainder of the section shows normal-appearing thyroid tissue making up the substance of the secondary tumor. (x 160)

FIG. 4.—Case 3: (S—46/1662) A vein in the wall of the primary adenoma, filled with tumor cells. In one corner can be seen normal-appearing thyroid acini filled with colloid. (x 65)

FIG. 5.—Case 3: (S—46/1662) High power showing a section of the vein wall with tumor cells filling the lumen and normal-appearing thyroid tissue on the outside. (x 300)

She received during the last year a total of four courses of deep roentgenray treatments to the thyroid gland and 5th thoracic spine area.

Her last admission to hospital was in April, 1946, for her 4th deep roentgenray series. At that time her thyroid gland was still enlarged—not showing much diminution in size since before her treatments. Her neuologic examination, however, revealed a very definite improvement.

Sensory involvement had completely returned from xiphisternum down to her knees, though remained somewhat impaired below that level.

Bladder function had returned to normal.

Motor power was not present in all muscle groups though still not sufficient to allow her to bear weight.

Case 5.—Mrs. W. C., female, age 30. This patient developed an adolescent goiter at the age of 12, which did not increase in size until November, 1941. A thyroidectomy was performed three months later because of pressure symptoms and the pathologic examination (2—42/469) showed thyroid tissue which, on the whole, was suggestive of a simple thyroid adenoma with some cystic degeneration, but the presence of a few small areas of atypical cell formation together with evidence of blood vessel infiltration with parenchymal cells, established the diagnosis beyond doubt of its malignant nature.

Two months later she noticed the gradually increasing development of a weakness and numbness of both lower limbs. Examination at that time showed an incomplete spastic paraplegia, paresthesia and some sensory loss involving the lower portion of her trunk and lower limbs. She could not get upstairs except by crawling on her hands and knees.

Radiologic examination revealed evidence of bone destruction of 7C and 1T. vertebrae and double spinal puncture established the presence of a complete block at that area.

A cervical laminectomy was performed May 26, 1942, and a bluish-purple, granulomatous mass, involving and softening the laminae of C7 and T1 and lying within the extradural space, was found. It was technically possible to only partially remove this tumor which, on section (M. P. 153-42), showed a typically benign type of thyroid tissue.

This patient was then given a total of five series of teleradium to the region of the cervicodorsal spine. She has shown gradual and steady improvement. She now works in a bottle factory, standing on her feet eight hours a day. Her stance and gait are normal. Sensory return has been complete. Other than an occasional aching pain in her left hip and calf noticed after a strenuous day, she has no complaints whatsoever.

DISCUSSION AND CONCLUSIONS

These cases well illustrate the main features of this condition and may be briefly summarized:

(1) The patient usually first comes to hospital because of symptoms produced by the bony tumor. In this way these cases simulate those of carcinoma of the prostate or of hypernephroma which frequently give signs of bony metastases before the primary new growth has been found.

(2) Despite the benign appearance of the histopathology of these metastaces, if a careful search is made, a malignant primary focus can always be found in the thyroid gland.

(3) This primary process is nearly always a well-encapsulated adenoma which for some unknown reason has become malignant, invading local blood vessels and spreading to some distant portion of the skeletal system *via* the blood stream.

(4) In our series only 33 per cent of malignant adenomata had formed

metastases by the time the primary growth was removed from the thyroid gland.

(5) Secondaries from this type of tumor have a predisposition for the osseous system in which to settle. The bones most likely to become involved are shown more accurately in Simpson's review of 77 cases. He reports:

Skull	30	Femur	9
Vertebrae	25	Ribs	9
Pelvis	11	Humerus	7
Clavicle	9	Scapula	3
Sternum	9	Mandible	2

(6) These metastatic tumors have a tendency to invade bone by growing in an expansile manner, erroding the bony cortex and giving a radiographic picture somewhat similar to osteolytic sarcoma or giant cell tumor.

(7) The bony metastases are frequently pulsatile and occasionally enlarge during menstruation and pregnancy, although this latter observation was noted in our series.

(8) No conclusion can be drawn from these cases in regard to the interesting problem of hyperthyroidism associated occasionally with these tumors. Case 1 had a B. M. R. of +37 which rose to +45 one month after thyroidectomy.

Reinhoff[9] states that "it is very unlikely that hyperthyroidism ever occurs in the absence of histologic evidence of hypertrophy and hyperplasia of the thyroid epithelium whether associated with a benign or malignant tumor. As a rule, the symptoms of hyperthyroidism accompanying malignant tumors of the thyroid are very mild.

Treatment.—Complete excision of the primary malignant adenoma and metastases would seem to be the most rapid and effective means of dealing with this problem. This we hope to have accomplished in Case 3, in whom the primary in the thyroid and the only demonstrable secondary, that involving the radius, were removed. Removal of the secondaries alone is not enough, as the primary, if left, will continue to give off metastatic emboli.

The effectiveness of this means of treatment depends on removal of both primary and secondaries early, before multiple secondaries make this procedure technically impossible. The slow growth of this tumor is in the surgeon's favor. Our cases suggest that one has at least a year after the formation of the first metastatic tumor, before others begin to develop. The importance of recognizing the malignant nature of this condition cannot be overemphasized.

Deep roentgenray therapy seems to have found a definite place in the treatment of this condition. There have, however, been an insufficient number of cases treated over too short a period of time to come to any definite conclusion as to the effectiveness of this treatment.

Case 1 continued over a period of three years, during which he received radiation, to slowly, but inexorably, deteriorate until his death, when autopsy revealed large and multiple metastases.

Case 4 has now been treated for one year, during which her symptoms of

cord pressure are markedly improved, although the thyroid gland is not much smaller. In this case, probably all that one can say is that the progress of her condition is being effectively held in check by radiation therapy.

Case 5 has received five courses of teleradium during the last four years and, so far as it is possible to tell at the moment, she is cured.

In conclusion, may I reëmphasize that as soon as a biopsy report reveals a bone tumor of this type, the surgeon must not allow himself to temporize because of the apparent benign appearance of the pathologic section, but must pursue an active and an effective course in eradicating both primary and secondaries, preferably by surgical means, or if this is not possible, by deep roentgenray therapy, for on early and adequate treatment, rests the patient's life.

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THE MECHANISM OF HEMOSTASIS

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THIS IS AN EXPOSITORY REVIEW intended to assemble the existing knowledge of blood and vascular physiology into a coherent working concept of the mechanism of hemostasis. An effort is made to bring to date and incorporate into a discussion of this mechanism, some of the facts brought out during the past ten years.

Petit[1] was among the first to call attention to the significance in the spontaneous arrest of bleeding from wounds, of the plugging mass formed from blood within and just outside the opening of divided vessels. Jones,[2] Ballance,[3] and Lister[4] studied the subject further, especially in relation to the hemostatic effect of vessel ligation. Hayem,[5] and Bizzozero[6] investigated the part played by platelets and other blood elements in sealing off defects in the wall of vessels. In more modern times, Stich,[7] and Schloessmann[8] have discussed the clinical aspects of the questions; Apitz,[9] Stegeman,[10] and Magnus[11] have dealt with its experimental physiology, and an historical account has been given by Harvey.[12] A critical review of hemostasis stressing the dominant rôle of vascular contraction in the arrest of bleeding from small vessels has been presented by Macfarlane.[13]

In recent years, research and discussion on the mechanism of hemostasis and its disorders have, with rare exceptions, been chiefly concerned with the coagulation of blood and properties of the clot.[14] The spontaneous arrest of bleeding involves more factors than those contributed by the blood alone. Severe disorders of hemostasis may exist in the presence of little, or no, obvious impairment of blood coagulation, sometimes even with an accelerated coagulability. Conversely, there may be a serious defect in blood coagulation with no apparent disorder of hemostasis, provided no unusual stresses are present.

The blood is normally kept within a system of intercommunicating vessels of caliber and walls of various dimensions, coursing through tissues of widely varied composition, exposed to different environmental conditions. The physiochemical state of the blood itself changes in its various locations, and there is, likewise, no uniformity in the behavior of the vessels in different parts of the body. It follows that, after a given injury, the amount of bleeding will vary according to the prevailing efficacy of the hemostatic mechanism in the involved area. Moreover, factors which contribute to the continuation of bleeding in one section of the body may have a negligible influence in another.

Any attempt, therefore, to give a general description of the mechanism of hemostasis is bound to result in an oversimplification of the facts. At least three groups of factors may be said to be engaged (actively or passively) in preventing or checking blood loss from the body. For convenience of discussion they may be divided into:

1. *Extravascular factors,* or those that are located or exert their action outside the vessels.

2. *Vascular factors,* or those located in the vessel wall itself.

3. *Intravascular factors,* or those residing within the vessel, or in the blood itself.

EXTRAVASCULAR FACTORS

Location of the Vessel.—If a vessel runs close to the surface, with little or no tissue intervening between the vessel and the air, it is at some disadvantage, insofar as hemostasis is concerned. This specially applies to vessels which run parallel to the surface, as in the mucous membrane of the nasal septum, with, on one side, a thin exposed mucous membrane and, on the other, a rigid surface. An injured arteriole in this location has little or no support on one side with an unyielding surface on the other. The escaping blood nearly always pours out into the nasal cavity, since the vessel meets with little extravascular resistance to aid it in closing the opening. The ease of development and occasional difficulty in the control of nasal bleeding may be partly explained on this basis. The small vessels coursing along the mucous or serous surface of the gastro-intestinal, respiratory or urogenital tract or of any other hollow viscera are, likewise, deprived of much support. It is not surprising that blood may escape from vessels in such locations, even after comparatively slight trauma. It is from them that bleeding often occurs in disorders of the hemostatic mechanism.

Tissue Tension or Elasticity.—The degree of tension in the tissue surrounding the vessel wall protects it from damage and aids it in resisting the flow of blood through the damaged site. Bleeding from small cuts of the skin may cease, before there has been any significant amount of blood lost, when the skin closes over the open vessels. The integument acts as a protecting cover for the vessels that run under it. Even the progress of large hemophilic hemorrhages may be eventually checked by the resistance offered by a distended overlying skin. In the aged and in those debilitated by prolonged illness, the loss of elasticity of the skin is largely responsible for the ease with which subcutaneous hematomas develop, as after venipunctures.

Vessels coursing through bone, ligaments, cartilage or other semirigid structures are well protected from injury because of the rigid support about them. Only severe stresses may injure their walls and lead to blood loss. The noncollapsible character of the tissue about such vessels may, however, delay hemostasis, when the rigid channel through which the vessels run is destroyed. The well known difficulty of stopping the oozing of blood from the cut-surface of bone is principally due to this. Plugging of the bony orifice may be required to check the bleeding.

The resistance offered by the tissues of the body to forcible distension of their spaces varies, of course, with the type of tissue. This resistance is known to oppose the loss of fluid from vessels, and it also influences the escape of blood from them. It operates, of course, at its best in overcoming blood loss from the smaller arterioles or from the venous circulation, where the blood pressure is of such a low order of magnitude that the tissue tension may offer effective opposition to it. The skin helps to maintain the blood within the

small vessels of the lower extremities, where it is often under high pressure. The practice of bandaging the extremities in edema, peripheral vascular failure, hemorrhage from ruptured veins is designed to supply this type of support to the vessels and, thereby, keep the blood within them.

The tissues of certain organs like the brain, offer little resistance to blood extravasations. If the ruptured vessel is an arteriole or larger, the hemorrhage may compress the tissue to dangerous proportions before it is checked. Wherever loose areolar tissue surrounds a vessel, it affords little resistance to extravasated blood. The subcutaneous tissue about the orbit, the antecubital and inguinal regions do little to oppose the escape of blood from surrounding vessels. The opposite is true in certain conditions, like scleroderma. The skin becomes abnormally tense and rigid and the vessels are so compressed that little or no blood emerges when the skin is cut.

The content of thromboplastic substances in the tissues may conceivably have some influence on the rapidity of the clotting of blood escaped from the vessels. It is largely because of its contact with the damaged vascular wall and surrounding tissues that extravasated blood undergoes the changes that precipitate clotting. The variable thromboplastic activity of extracts of different organs may indicate that the tissues do vary in their content of clot-accelerating substances. Anticoagulant materials are also found in the tissues in varying concentration and potency, apparently side-by-side with thromboplastic substances. Tissue autolysis will often destroy the clot-accelerating substances and, thereby, enhance the action of the clotting inhibitors. The stability of blood extravasated into the tissues, therefore, depends to some extent on the type and condition of the tissues with which it comes in contact.

VASCULAR FACTORS

Structure of the Vessel.—This obviously influences the arrest of bleeding. Arteries and arterioles have relatively thick elastic walls which protect them from fairly severe stresses. Since the pressure of the blood within these vessels is high, much blood is usually lost, however, before a defect in the vessel wall is corrected. A break in the wall of a large artery calls for the rapid, combined action of all hemostatic forces. Patients with other than vascular defects in the hemostatic mechanism may suffer little or no inconvenience from an injury to a small vessel, but may be seriously handicapped when large arteries are involved. The thin walls of capillaries and venules afford little protection from trauma, but these vessels carry less blood and are more susceptible to external influences (tissue tension and pressure). In health, the thin walls of capillaries and venules can stand moderate increments in intravascular pressure for a short period of time, but may be incapable of supporting long-sustained sudden rises as, for example, after the application to the arm for 15 minutes of a tourniquet tight enough to check the venous return.

The walls of the larger veins are structurally strong, elastic and able to contract when injured. In general, veins are easily displaced, distended and compressed without injury. The thinness and flexibility of the walls of veins render them readily influenced by the hydrostatic pressure of the blood within

them. Given favorable conditions, loss of blood from veins may be checked by compression of surrounding tissue, by reduction of the hydrostatic pressure within the vein and by clotting and other changes in the blood. When the wall of a vein is distended and weakened by disease and the venous pressure is abnormally high, there may be difficulty in arresting bleeding (*e.g.,* esophageal varices).

Certain functional attributes of the walls of blood vessels, namely, their retractility and contractility, are among some of the most important factors in this mechanism. In health, the elastic and muscular coats of vessels render them distensible and contractile. These properties are used principally to vary the caliber of the vessel, thereby regulating the amount of blood flowing to a part and the resistance offered to the flow.

Contraction of the muscle coats and retraction of elastic fibers are probably natural responses of the wall of some vessels to mechanical injury. This response may be due simply to the properties of the vascular tissue itself. Aside from this, most vessels including the capillaries, are under the influence of sympathetic innervation, as part of an intricate system of reflex vasomotor pathways, as yet not thoroughly understood. The contraction of vessels that follows, for example, exposure to cold, explains in part the *temporary* hemostatic effect of this physical agent. Heat (40°–60°C.) generally produces vasodilatation and would, *if this were its only effect,* favor bleeding.

The elasticity of the wall of larger vessels protects them from excessive internal and external stresses and aids them, when injured, in retracting their walls and reducing their lumen. For example, after a large vessel, like an artery or vein, is severed, the intima is often rolled-in, and the two ends of the vessel retract away from each other. In gunshot wounds of the large arteries, the adventitia of the vessel may show only a tiny opening, while the intima may be torn away widely and rolled-up rosette fashion. Segmental spasm of the vessel, contraction and retraction of the vessel wall and puckering of the intima, all contribute to the initial efforts to stop blood flow from an injured vessel.[7,9,10] The retracted intima not only narrows the lumen of the vessel but offers a suitable surface for the accumulation of platelets and a foundation for the clot. If circular as well as longitudinal contraction of the vessel is maintained long enough, the flow of blood is reduced or perhaps arrested, and enough time is afforded for the laying-down of the clot, its hardening, adhesion to the vessel walls and retraction. If vasodilatation occurs before coagulation is well under way, the as yet soft clot might be blown-out and bleeding resumed. If the vessel remains dilated after being severed, a longer time is required to build up an effective, obstructing clot. If, on the other hand, coagulation is delayed, no clot will be laid-down during the early phase of vessel contraction and the eventual relaxation of the vessel will find its lumen still patent. Prompt hemostasis clearly depends on the effective *synchronized* action of severed vascular and intravascular factors.

INTRAVASCULAR FACTORS

The Hemostatic Plug.—This term designates the blocking mass which is

formed at any point in a vessel wall where a defect exists, thereby preventing potential, or arresting existing loss of blood through the defective area.[5,6] This plug may consist of platelets alone, fibrin, white cells, red cells, or all in combination. Fibrin may not necessarily be present. The plug may be a simple mass against the wall of the vessel (mural thrombus) or project into the tissues through the opening in the wall. Arrest of bleeding depends in a large measure on the formation of this plug by elements from the blood itself. Formation of the plug may be separated into three phases, each of which may occur independent of the other or fail to appear altogether:

1. Platelet Massing: Platelets from the blood are attracted to the damaged zone, come together, adhere to, and form a layer over the area.

2. Deposition of Fibrin: A network of fibrin is formed, trapping the formed elements and arresting blood flow.

3. Contraction and Hardening of the Platelet/Fibrin Plug: The fibrin and platelet network increase in density, and serum and some of the trapped cells are released.

1. *Platelet Massing.*—This is probably the simplest form of reaction of the blood to an injury of the vessel wall.[5,9] It may be the only reaction to an injury in small vessels (capillaries, venules) where the blood pressure and volume are relatively low and the vessel walls thin and collapsible. Platelet massing occurs on vessel walls in contact with a moving stream of blood, from where the platelets obviously must come. If the column of blood is stagnant, only nearby platelets are drawn to form the clump against the wall. When the injured area is in the intima lining the cavities of the heart or the walls of large vessels and, therefore, in contact with large, rapidly moving columns of blood, the mass may assume great proportions (endocardial mural thrombus, thrombosis of aneurysmal sacs).

Platelets are small (1–4 microns in diameter) thin, round or oval bodies, circulating, most times, singly in the blood. When exposed to certain conditions (in a coagulating medium or in contact with favorable surfaces), they come together and adhere to each other or to the contacting surfaces. The clumped platelets may then swell, burst and liberate substances (cephalin-rich) with clot-accelerating properties. The remainder of the mass becomes granular, shrinks, and may remain fixed to the surface. A thin fibrin film may then be deposited at the point of contact between the platelet mass and the overlying blood. Other platelets in blood flowing by, adhere to the fibrin film and form about it clumps which may themselves undergo the changes just described.

Platelet massing requires, obviously, that there be (a) an adequate supply of platelets with the (b) proper degree of agglutinability and capacity for adhesion to certain foreign surfaces. This at once suggests that quantitative or qualitative deficiencies in the platelets might be expected to give rise to a disorder of hemostasis manifested principally in the capillaries and venules. Moreover, one may expect that when the rate of blood coagulation is delayed but the platelets are not altered, hemostasis in these small vessels may not necessarily be altered.

The number of platelets in the peripheral circulation depends on several

factors, among which are (a) the rate of platelet production; (b) the rate of platelet utilization or destruction; and (c) the distribution of platelets in vessels in various parts of the body.[15] Platelets originate from megakaryocytes, the large multinucleated cells found principally in the bone marrow. The granular cytoplasm of these cells projects into the sinuses of the marrow, becomes constricted and the segments are probably broken off by the impact of the blood stream, thus giving rise to the platelets. How this process is started, accelerated or adjusted to the needs of the body is not known. The normal rate of platelet production is probably 100,000 platelets, per cm. of blood per day, judging from the time required for the number of platelets in the peripheral blood to return to normal after natural and experimentally induced thrombopenias. Accelerated platelet production and the presence of giant platelets often follow acute and chronic hemorrhage.

Platelet utilization and destruction are intimately linked, since, when the platelet is used, it is, unlike the erythrocyte, nearly always destroyed. There are indications that some of the platelets are destroyed in the spleen (and perhaps other organs). Just how this takes place and how it is regulated is not clear. There is no *direct* way of establishing whether or not an increase or decrease in platelet destruction is taking place; inferentially, if there are reasons to believe that the rate of platelet production is normal or accelerated, a thrombopenia may be taken to be the result of an increase in platelet destruction.

Generally speaking, the utilization of platelets increases whenever the body is exposed to excessive stresses (trauma, most infections). During the acute period of most bacterial infections (pneumonia, diphtheria, variola, typhoid, scarlet fever, meningitis) and immediately after fractures or major surgical procedures, there is a thrombopenia, which is perhaps chiefly the result of increased utilization but may be due as well to decreased production of platelets.[15] The reverse takes place when the acute period of the illness is over, or 2–10 days after fractures and operations, when the number of platelets may increase two or more times above the normal figure.

The distribution of platelets is not uniform throughout the vessels of the body. There are more platelets in arterial than in venous blood of the extremities,[16] and differences seem to exist in the platelet content of vessels in various organs. When a deficiency of platelets exists, its effects would be expected to appear in areas where platelets are normally in lower concentration.

The Clotting of Blood.—Deposition of fibrin may or may not follow platelet massing at the damaged area of the vessel wall. Fibrin formation is probably going on continually in the body as part of the mechanism of repair of tissues. Fibrin is laid outside the vessels almost as frequently as inside, to serve other than hemostatic purposes, perhaps as scaffolding along which building or reparative processes are directed or initiated.

In vessels where the pressure or volume of blood are high, much of the effectiveness of the hemostatic mechanism depends on (1) the rapidity with which the fibrin clot will form; and (2) the promptness with which that clot will become dense, adhere to the vessel wall and retract itself. Let us first direct our attention to the factors which govern the rate of fibrin formation.

The Rate of Blood Coagulation.—In order to understand what makes blood clot when shed outside the vessels, it is important, as well, to know what keeps it fluid while in circulation. Fluidity and coagulability are, in a sense, antagonistic to one another. Both physical states are essential in their proper places. Excessive bleeding may result when blood is so stable that it remains liquid longer than it should after it leaves the vessels; if, on the other hand, blood clots within the vessels, where it should not, an interruption of the circulation may follow. It is by keeping a balance between fluidity-inducing (anticoagulant) and coagulation-promoting (coagulant) factors, that the blood maintains itself as a circulating medium.[17] Blood seems to contain within and about itself all that is required to delay or promote coagulation. The stability of blood (with respect to coagulation) depends on which of the two following groups of antagonistic factors is dominant over the other:

ANTICOAGULANTS (Fluidity-promoting Agents)	COAGULANTS (Coagulation-promoting Agents)
1. Intact vascular endothelium (or a surface like collodion film)	1. Damaged vascular endothelium (or a surface like clay or glass)
2. Anticephalin (antithromboplastin)	2. Cephalin (platelets, leukocytes, tissue juices)
3. Antithrombin	3. Prothrombin Ca^{++}
4. Fibrinolysin	4. Fibrinogen.

The coagulability of a given sample of blood is enhanced when there is an *uncompensated* increase in the effective amount of the coagulation-promoting factors or a decrease in the fluidity-promoting elements. Conversely, blood may become unusually stable if there is an *uncompensated* increase in anticoagulants or decrease in the coagulants.[17]

An example may help in clarifying the above concept. If an excess of tissue extract (thromboplastin) is added to 1 cc. of normal blood, its rate of clotting may be reduced from about 10 minutes to 30 seconds, or less. Here, the hypercoagulability resulted from an *uncompensated* excess of cephalin. In contrast, if venous blood is collected from a hemophilic and allowed to stand in a glass tube, it may not clot for several hours; its stability is due to the excess of anticephalin activity, while all other factors have remained normal.

The changes that occur in the blood after it is shed and brought into contact with foreign surfaces may be divided into three phases:

First Phase.—Release of cephalin (as such or in the form of thromboplastic lipoprotein) from platelets, leukocytes and possibly injured tissue in the area surrounding the damaged vessel. Reduction and eventual loss of the natural anticephalin activity of the blood when it comes in contact with the released cephalin or the damaged surface of the vessel. The normally slow reacting prothrombin is made thereby highly vulnerable to the action of cephalin. These steps may take place simultaneously or one may precede the other, depending on prevailing conditions.

Second Phase.—Transformation of prothrombin to thrombin. The rate of formation of thrombin depends on the amount of cephalin available and the extent of anticephalin activity. The quantity of thrombin formed depends on the amount of prothrombin available.

THIRD PHASE.—Action of thrombin on fibrinogen with production of fibrin. The rate of fibrin formation depends chiefly on the amount of thrombin available; the quantity of fibrin formed varies according to how much fibrinogen is present. Any excess of thrombin is inactivated by antithrombin. The clot is eventually liquefied by the action of fibrinolysin.

In normal blood the steps may be represented as follows:

1. Prothrombin (bound or protected by anticephalin)	+	Cephalin or suitable contacting surface	=	Free prothrombin
2. Cephalin	+	Free prothrombin	=	Thrombin
3. Thrombin	+	Fibrinogen	=	Fibrin
		Antithrombin	=	Metathrombin (inert)

The Contacting Surface.—The interior of a blood vessel is lined with endothelium, which offers to the blood a neutral contacting surface, neutral in the sense that it will neither precipitate the changes that precede the inception of clotting of blood, nor supply any substances to maintain its fluidity. As long as blood contains an adequate amount of clot-inhibiting substances and the vascular surface remains intact, the stability of circulating blood will be unaltered. When the surface is damaged, that stability is threatened by:

(a) The presence of cephalin-rich tissue juices which help to neutralize the blood anticephalin activity and to accelerate the conversion of prothrombin to thrombin.

(b) The changes in the physical properties of the surface in contact with the blood. The damaged surface helps to remove anticephalin from the blood, besides aiding in the disintegration of platelets and leukocytes and the consequent release of more cephalin. Surfaces like collodion films behave toward the clotting of blood somewhat like the intact vascular endothelium, while surfaces like glass or clay behave like damaged tissue surfaces.

Cephalin: This term serves to designate the lipid or group of lipids with clot-accelerating properties which form the active component of thromboplastic tissue and platelet extracts. Cephalin is found in most tissues of the body, but especially in the brain, lung, heart and testicle. In the blood itself, this clot-accelerator is found chiefly in the platelets and leukocytes. On account of their small size, relatively larger numbers and general distribution, platelets offer an extensive contacting surface, important attributes in areas where surface conditions are favorable to their agglutination and disintegration. On disintegration, platelets release cephalin which is thereby dispersed through the blood and initiates the changes in immediately neighboring areas that eventually lead to the formation of thrombin. The number of platelets in the blood (200,000 to 400,000 per cm. of blood) is about 40 times the amount required to accelerate the coagulation of normal blood. There may, therefore, be a great decrease in the number of platelets without much change in the rate of coagulation, other things being equal. Irrespective of their number, the rate of disintegration of platelets must also be taken into consideration. The two most important factors that influence platelet disintegration are the coagulability of the plasma in which the platelets are suspended and the extent of contact with surfaces favoring their disintegration. If, for example, the contacting surface is like paraf-

fin, and the plasma is rich in clot-inhibiting substances, there may be little or no change in the platelets for some time after the blood is shed. There is no conclusive evidence that a defect in the platelets themselves may be responsible for their occasionally observed slow rate of disintegration.

Anticephalin (or Antithromboplastin) Activity.—When suspensions of human cephalin or cephalin-containing substances (*e.g.*, tissue extracts containing the thromboplastic lipoprotein) are incubated with normal human plasma in plastic or collodion-coated tubes, their clot-accelerating power is gradually reduced. To this property of human plasmas, the term anticephalin (or antithromboplastin) activity has been applied.[17] To this activity is probably due the protection enjoyed by the circulating prothrombin against being activated by the cephalin (or cephalin-containing thromboplastin) released from platelets and tissue cells. Little, as yet, is known regarding the nature, source and mode of regulation of this activity. It seems to decrease when blood is brought into contact with surfaces like glass or with blood cells or débris of tissue. Hemophilic blood contains an excess of this activity,[17] while blood from normal men after a severe hemorrhage seems to owe its hypercoagulability to a diminution in anticephalin activity.[17] The natural anticephalin activity of the blood is greatly potentiated by the addition of substances like heparin, which, by itself, (*i.e.*, without the aid of plasma cofactors) have no effect on the clot-accelerating action of cephalin.

Prothrombin.—This substance, a protein with many of the characteristics of the euglobulins, is probably the clotting factor about which the greatest amount of information is available.[18] It is formed almost exclusively in the liver, and in its synthesis the participation of vitamin K is required. Prothrombin is identified by its activity, that is, by its capacity to form thrombin, since its chemical characteristics, not to speak of its identity, are still largely unknown.

The amount of prothrombin in the circulating blood is, like that of any other substance in the circulation, an expression of the equilibrium between the rate of production and delivery of prothrombin into the blood and the speed with which it is used up or destroyed. There is a 5- to 10-fold excess of prothrombin over the amount required to bring about prompt coagulation of blood. Other factors remaining equal, a diminution to about 10 per cent of normal, or below, is necessary before a significant change is observed in the rate of clotting and the quality of the clots formed. This diminution may result from:

(a) Increased utilization of prothrombin, as after widespread trauma or prolonged illness.

(b) Imperfect synthesis of prothrombin by the liver (*e.g.*, cirrhosis of the liver).

(c) Improper digestion or absorption of an otherwise adequate diet (*e.g.*, obstructive jaundice, intestinal obstruction).

(d) Deficient intake of vitamin K, usually observed along with other nutritional deficiencies.

(e) The effect of certain drugs (barbiturates, salicylic acid and its salts, dicoumarol).

(f) A poorly understood disorder designated congenital idiopathic hypoprothrombinemia.

In any one clinical condition the hypoprothrombinemia often results from operation of two or more of the factors mentioned above. For example, in an acute infection, such as lobar pneumonia, the diminution in prothrombin results perhaps from increased utilization, depression of hepatic function and diminution of the amount of vitamin K in the diet.[19]

Increases in prothrombin activity above normal are usually observed in the latter months of pregnancy,[18] and following the administration of epinephrin.[20]

Fibrinogen.—Fibrinogen is the blood protein which, when acted upon by thrombin, is transformed into fibrin. Like prothrombin, fibrinogen is formed principally in the liver. The amount of fibrinogen in the plasma is usually determined by allowing the plasma to clot, and measuring the protein content of the clot. From 180 to 400 mg. per 100 Ml. is the normal range of fluctuation of the plasma fibrinogen. Little is known concerning the mode of production and the substances required for the formation of this protein. As with prothrombin, fluctuations in the fibrinogen content result from adjustments between its rate of production and utilization. Certain infections, especially those accompanied by much suppuration, lead to high increases in plasma fibrinogen. In disorders of the liver accompanied by much functional impairment (such as chloroform, carbon tetrachloride poisoning, acute yellow atrophy) diminution in the fibrinogen of the blood is observed. Blood of high fibrinogen content yields dense, tough clots, while in fibrinogenopenia the clots are thin, friable and ineffective. There are indications that qualitative defects in the fibrinogen render it less readily clotted by thrombin and influence the physical characters of the fibrin formed.

Fibrinolysin.—This term serves to designate an agent which brings about dissolution of the fibrin formed intravascularly, or extravascularly, during coagulation. The liquid state of cadaver blood is said to be partly due to the action of fibrinolysin and serum tryptic enzymes. Fibrinolysin seems to exist in the plasma in a precursor state, profibrinolysin, requiring activation before its full proteolytic function can be performed.[21] Fluctuations of this enzyme-like substance apparently take place in various disease states. especially when the fibrinogen content of the blood is increased and there is much laying-down of fibrin, as in pneumococcic lobar pneumonia. The blood of women during the first days of menstruation has an increased fibrinolytic activity which may have its source in the endometrium. Beyond the existence itself of fibrinolytic activity in the blood, little else of a definite nature is known concerning its site of origin, rate of output and eventual fate.

Antithrombin.—Normal blood has the capacity of offsetting to a certain extent the coagulating action of thrombin. To this property the term antithrombin has been given. The designation should be reserved for that anticoagulating activity of the blood directed towards thrombin itself. The activity appears to reside in the albumin fraction of the plasma or a constituent closely associated with that fraction. The union between thrombin and this albumin constituent leads to the formation of metathrombin, an inert product, insofar

as clotting is concerned. Under normal conditions, the antithrombin of the blood probably plays a minor part in slowing the rate of coagulation since, if fibrinogen is available, the formed thrombin will change it into fibrin before it can be inactivated by antithrombin. Plasma can be clotted by an amount of thrombin which is only 1/2,000 of the quantity which would be inactivated by antithrombin in five minutes, were fibrinogen absent.[14] Antithrombin may, nevertheless, serve the purpose of removing the excess of thrombin accumulated in an area where clotting has taken place, thereby preventing thrombin in high concentrations from reaching neighboring areas of the circulation. Antithrombin originates perhaps chiefly in the liver. A potentiation of the antithrombin activity of the blood may be brought about by the addition of substances like heparin and hirudin.

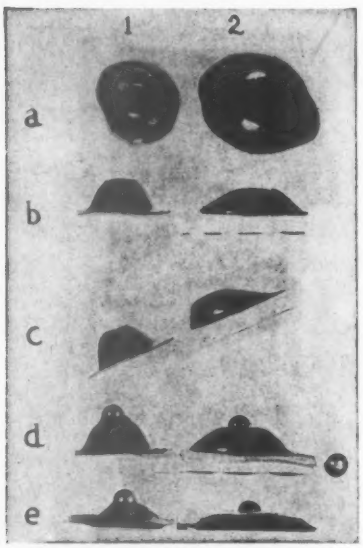


FIG. 1.—Physical Characteristics of Clots from Normal (1) and Thrombopenic (2) Blood. The clots (8 cc. of dog blood) were removed from a conical porcelain cup where they were formed.
(a) Viewed from above.
(b) Lateral view.
(c) On an inclined plane.
(d) After placing a steel ball (Wt. = 1.5 Gm.) on the surface of the clots.
(e) Twenty-four hours afterwards.
The thrombopenic clots are bulkier, softer, retain the fluid within their meshes and are more easily displaced, compressed and fractured than the normal clots (reproduced from Am. Jour. Physiology[22]).

HARDENING AND CONTRACTION OF THE HEMOSTATIC PLUG

In order to be effective the hemostatic plug must be formed promptly and meet certain physical requirements. During and after formation of the plugging mass, some of its physical attributes are gradually developed. These attributes, without which the effectiveness of the mass is much reduced, are: (1) Adhesiveness; (2) rigidity (resistance to distortion); and (3) contractility. The mode of development of these properties and the factors responsible for them are not entirely clear. Nearly all the factors mentioned above which influence the rate of coagulation of blood have some effect on the development of these properties. The promptness of their appearance is partly conditioned by the changes that precede the formation of the plug itself (Fig. 1).

Adhesiveness.—Aside from the fact that the adhesiveness of an hemostatic plug varies according to the type and extent of the surface with which the plug is in contact, there are certain changes in the composition of the plug itself which influence its adhesiveness to that surface. An adequate number of normally functioning platelets is one of these factors; thrombopenic clots are known to adhere little to the surrounding container. The platelet massing which often occurs at the interface between blood and contacting surface favors anchoring of the plug (Fig. 6). In the absence of platelets the plug may be easily displaced by the blood current. Moreover, as blood coagulates, its

viscosity and adhesiveness increase rapidly. At a certain phase of the transformation to fibrin (so-called profibrin) the fibrinogen becomes sticky; to this change in the fibrinogen may be attributed the tendency of coagulating blood to adhere to surrounding surfaces.

Rigidity.—(Resistance to Distortion): The development of this property of the clot depends principally on the amount of fibrinogen present and to a lesser extent on the number of blood platelets. The cellular composition of the blood also obviously influences the rigidity of the clot. Bloods with high fibrinogen content yield tough, dense clots, which are effective antagonists to the pressure exerted on them by the blood current. Normally functioning platelets in adequate numbers strengthen the internal structure of the clot by clumping about and binding the fibrin needles to each other.[22] Blood of low fibrinogen content yields flimsy, thready clots, easily displaced by the blood current. Similar clots are formed when the precipitation of fibrinogen is delayed or slowed by lack of thrombin or the presence of an excess of antithrombin or anticephalin. When the number of platelets is low or of defective quality, soft, friable clots may be formed.

Contractility.—Like other gels, the human blood clot shrinks and expresses most of the fluid that it contains. Some physiologic significance may be attributed to this property of the hemostatic plug. As ordinarily observed in glass vessels, contraction of a clot derived from 1 cc. of blood usually begins one-half hour after completion of coagulation and progresses slowly for two hours. In living vessels, however, conditions differ. Contraction probably begins almost immediately after the hemostatic plug is formed, since in most instances the plug is slender and tightly adherent to the surface of the vessel. The drawing together of a clot is furthermore aided by a collapsible vessel wall. Retraction of the plug pulls the vessel walls together and reduces the size of the orifice. Resistance to the flow of blood through the end of the vessel is further accentuated by the increasing density and rigidity of the clot.

The rapidity of clot retraction is prominently linked with the number of intact platelets left in the center of the clotting mass and with the amount and quality of the fibrin formed (Fig. 2). Other important factors influencing this change are the cell content of the blood (the greater the number of red cells, the less the degree of retraction) and the ratio of the mass of the clot to its surface area (thin clots with a wide surface retract relatively faster than thick clots with a comparatively small surface).[23] As illustrated in Figure 2, fibrin in platelet rich plasma is laid down first as needles which are later bound together by platelets agglutinating about them. Partly as the result of the binding of these needles and partly because of their natural tendency to shrink, the needles are brought closer together and slacken into a network of threads.[22]

As may be gathered from the above remarks, nearly every factor that influences the rate of blood coagulation will also influence the quality of the clot formed. Generally speaking, the faster the blood will clot, the more rapidly it will develop the physical attributes of contractility, adhesiveness and rigidity. Even slow-clotting bloods like those of hemophilics will, however, eventually display these attributes *"in vitro"* if enough time is allowed for their appear-

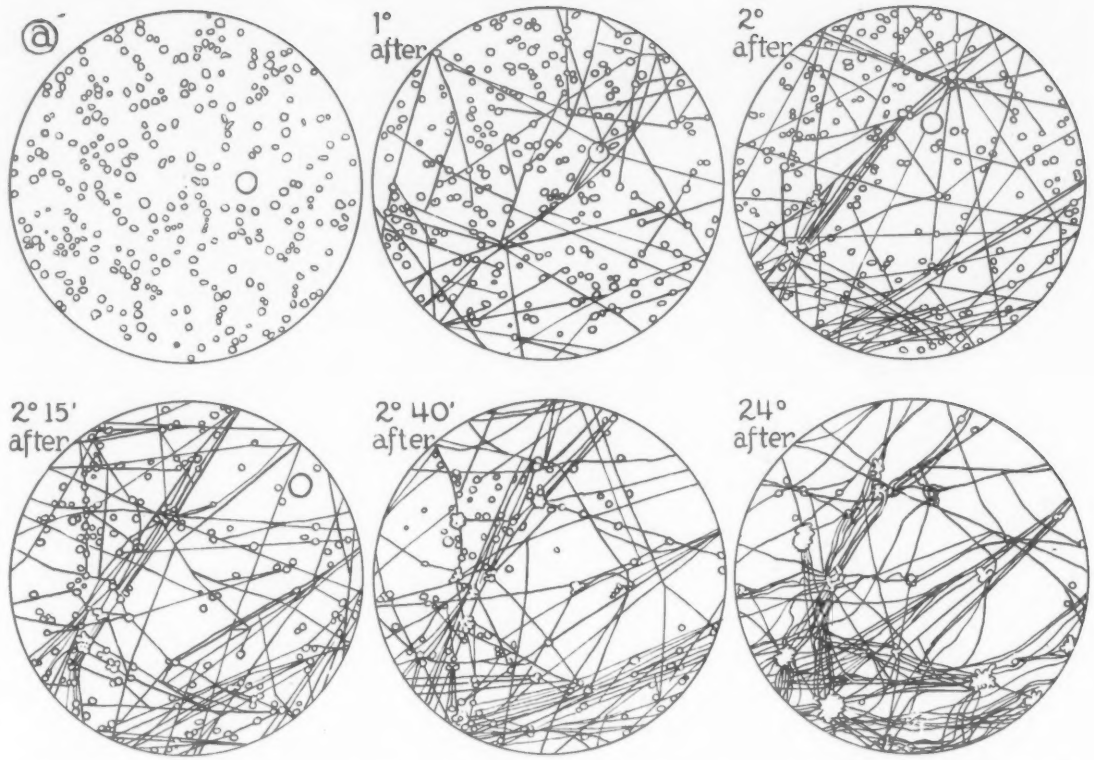


FIG. 2.—Microscopic appearances of different stages of fibrin formation. The fibrin is first deposited as needles to which the surrounding platelets adhere, forming clumps at the intersections. Shrinking of the clot is accompanied by slackening of the fibrin needles into bundled threads. In thrombopenic clots the platelet knots are absent and the fibrin is in the form of short, thin, loose needles (reproduced from Am. Jour. Physiology[22]).

ance. *In vivo,* the slowness of their development is what renders these clots ineffective in arresting hemorrhage.

THE DYNAMICS OF HEMOSTASIS

With the foregoing in mind, let us see, now, if we can give a general continuous account of the hemostatic mechanism. The spontaneous arrest of bleeding involves nearly always two phases which take place regardless of the type of vessel involved:

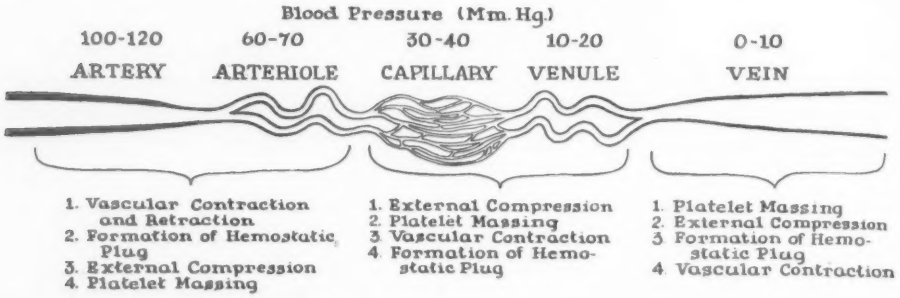
First Phase (Vascular): Immediately after blood begins to escape from a vessel, the pressure within it drops, the vessel walls tend to come together (contraction, retraction or simple collapse), and, if the blood is escaping into the tissues, the surrounding tissue tension increases. The increasing resistance to the flow of blood within the vessel causes the mass of blood to be routed through adjoining vessels. This all tends to reduce blood flow from the injured vessel and may, if the vessel is small and in a favorable location, be all that is needed to control the bleeding. Contraction of the walls, with occlusion of the vessel lumen, may last for days sometimes, but generally only a few minutes.

Second Phase (Hematogenous): The relative slowing of blood flow during the first phase affords it the chance of coming into contact with extravascular tissues or the damaged vessel wall, and precipitates the changes which lead to the plugging of the injured area (massing of platelets and/or a fibrin clot). The longer the first phase lasts, the greater the chance for these changes to take place. They may progress, however, even though blood flow has been reëstablished.

The order of succession, duration and magnitude of the changes included in these two phases vary considerably according to the type, caliber and location of the vessel, or vessels, involved and the volume, pressure and other properties of the blood within. So far as the blood is concerned, there is little information about changes in its composition in different parts of the body that might affect the functions under discussion. Arterial blood of the systemic circulation seems to have a higher platelet content that venous blood.[16] It is conceivable, therefore, that the hemostatic mechanism is at a higher level of performance in arterial blood. These advantages are offset, however, by the fact that, given a uniform wound, the volume of blood lost per unit time from an artery is much greater than from a vein, because of the obvious differences in pressure and rate of flow of the blood in the two vessels.

Another variable introduced by the changing caliber of the vessels is that the rate of clotting of a given mass of blood varies inversely as the extent of the surface in contact with the blood. One cubic centimeter of blood placed in a glass tube 5 mm. in diameter usually clots 2-3 times faster than in a tube 15 mm. wide. Generally speaking, the greater the surface in contact with a given amount of blood, the faster the coagulation. Likewise, the chances for adhesion of the clot are greater, if the blood is spread over a large surface. In the capillaries, this relationship works at its best. The volume of blood is small, while the surface in contact with the blood is large. Unless the blood is almost incoagulable (clotting times over 12 hours) or other defects (vascular

or extravascular) are present, the contacting surface plays a dominant rôle in initiating coagulation, besides supplying thromboplastic substances (from tissue surrounding the damaged vessel) and much space for the massing of platelets and adhesion of the clot. The reverse operates in large vessels, the arteries especially, where the ratio of blood mass to contacting surface is relatively greater. This partially explains why, when a superficial cut of the



PROBABLE ORDER OF IMPORTANCE OF THE COMPONENTS OF HEMOSTASIS IN DIFFERENT VESSELS

FIG. 3

skin is made, as for a bleeding time determination, there may not be excessive bleeding, even though the blood clotting time is greatly prolonged.

The structure of the vessel and the pressure of the blood within it, determine to a great extent the relative importance of each of the hemostatic factors. In large vessels, the volume of blood and the pressure it exerts per unit area and time is too high to be overcome by the simple deposition of a mass of platelets at the opening. It is necessary that the hemostatic plug be firmer and more closely knit; the laying down of fibrin and trapping of leukocytes, erythrocytes and further platelets in its meshes helps in providing additional strength to the plugging mass. In Figure 3 is shown the probable order of importance of the component steps of hemostasis according to the type of vessel involved.

In Figure 4 is illustrated in diagrammatic fashion the various steps in the arrest of bleeding from an artery severed across in an open wound. Substantially the same changes take place when the wall of the artery ruptures while the surrounding tissue is undamaged. All of the blood is naturally lost into the adjacent tissue and the mounting tissue pressure will play a more important part in the eventual arrest of the flow than when most of the blood is lost to the outside. There is also a better opportunity for the building up of the hemostatic plug than when the severed vessel is in an open wound; ligature of the vessel or packing of the wound may then be necessary to arrest the flow.

In Figure 5 are illustrated diagrammatically the steps in the spontaneous arrest of bleeding from a thin-walled capillary, ruptured or severed within the tissues. At this level, the eventual dominance of tissue pressure over blood pressure probably plays the leading rôle in checking hemorrhage. Massing of

platelets at the injured site aids in rendering hemostasis permanent. The drop in capillary blood pressure in the affected segment is what may lead to collapse of its walls; the rise in tissue pressure about the severed ends of the capillary aids in maintaining the collapse.

In Figure 6 are illustrated the steps in hemostasis of perforating defects of the walls of veins. Massing of platelets at the injured area and pressure of surrounding tissue are probably chiefly responsible for the repair of such defects. In the veins, hemostasis is further favored by the low or negative pressure of the blood within these vessels. Massive blood loss seldom results from single lacerations of a normal vein holding blood at ordinary pressure. The blood extravasations that are often attributed to the puncture of veins are

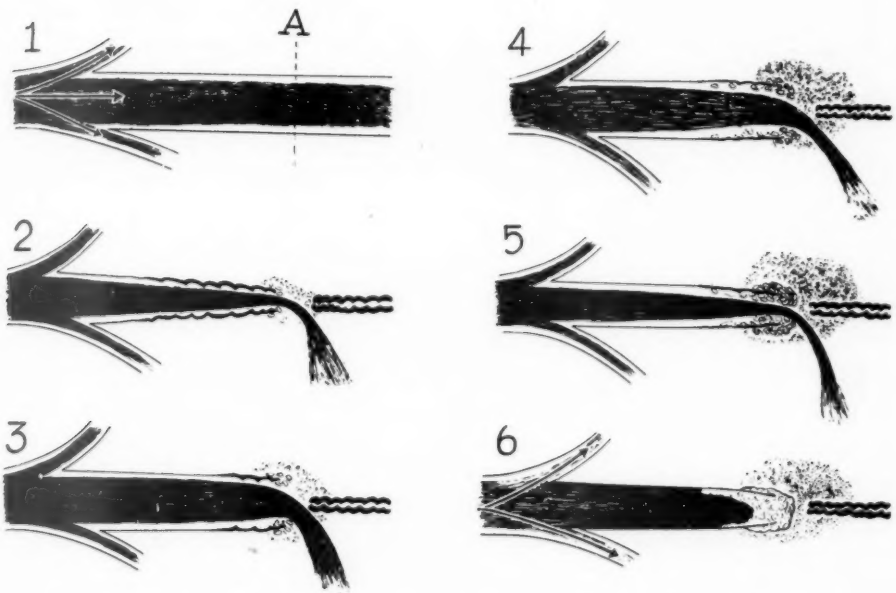


FIG. 4.—Diagrammatic Representation of Hemostasis in a Severed Artery in an *Open* Wound.

(1) After the vessel is severed at point A there is:

(2) Collapse, contraction, retraction and twisting of the distal segment. Contraction of the walls of the proximal segment and some longitudinal retraction. Temporary cessation of blood flow, depending on the degree and duration of the contraction. (Spasm of the vessel may continue for hours, and by the time dilatation occurs, an effective plug will have been formed inside the vessel and about its external end.) Infiltration of the surrounding tissues with part of the extravasated blood. Laying down of a platelet and perhaps fibrin layer at the edges of the vessel.

(3) Partial dilatation of the proximal segment of the vessel and consequent increase in blood flow. Infiltration of blood about the ends of the vessels. Continuation of the massing of platelets. Drop in blood pressure in the proximal limb due to sudden loss in peripheral resistance.

(4) Reduction in the lumen of the bleeding vessel by the growing platelet and fibrin mass.

(5) Further growth of the platelet/fibrin plug. Clotting of the blood extravasated into the tissues about the severed ends of the vessel.

(6) Complete occlusion of proximal severed end by a platelet/fibrin/red cell plug. Stasis of blood trapped behind the hemostatic plug. Diversion of the blood current into adjoining collateral vessels.

generally due to unintentional injury of small neighboring arterioles which are the true sources of most of the extravasated blood.

GENERAL DEDUCTIONS

A few general deductions may be drawn from these considerations:

(a) The nature of the defect in hemostasis determines to a large extent what vessels will be affected and these, in turn, the location and type of hemorrhagic manifestations. For example, the delayed blood coagulation in hemophilics leads to hemorrhage after an injury to large vessels (arterioles, arteries)

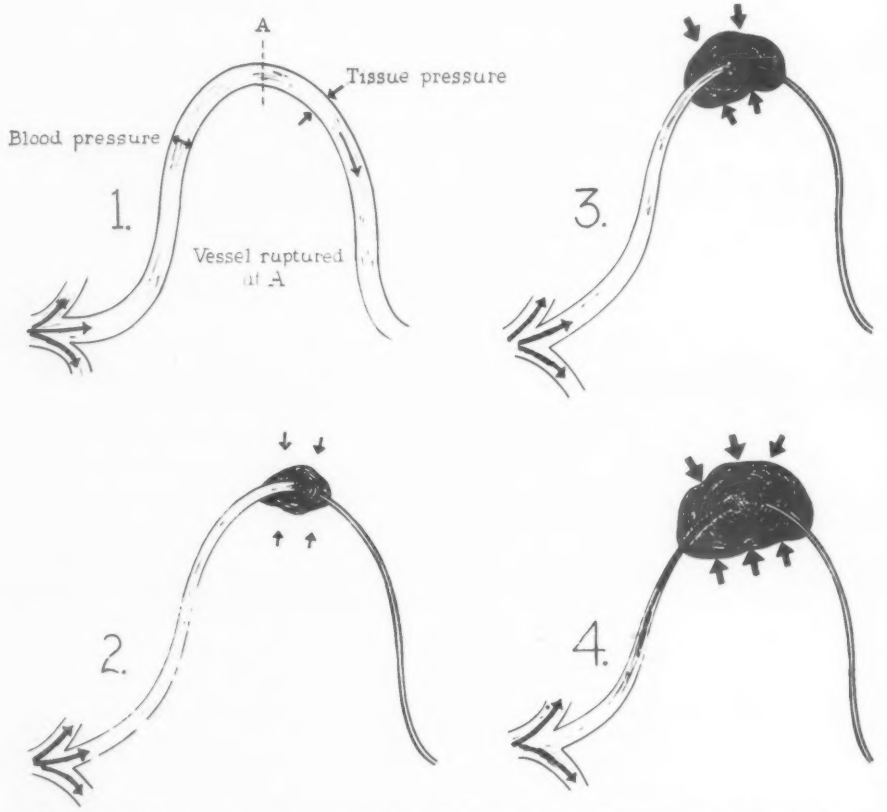


FIG. 5.—Diagrammatic Representation of Steps in the Spontaneous Arrest of Bleeding from a Ruptured Capillary within the Tissues. The entire process may take only a few seconds.

(1) Dominance of capillary blood pressure over tissue pressure maintains the vessel distended and filled with blood. When the vessel is severed at point (A):

(2) Blood escapes through the opening; distal segment collapses and becomes almost bloodless; the pressure in the proximal segment drops and the caliber of the vessel is reduced; blood infiltrates into the tissues about the severed ends of the capillary.

(3) Tissue pressure about the ends of the capillary rises as the extravasated blood distends the tissue; caliber of the proximal end of the vessel is further reduced due to external compression; platelets accumulate at the severed ends of the narrowed vessel.

(4) Tissue pressure continues to rise and the accumulated platelet mass reduces the opening of the vessel until the blood ceases to flow out; blood that had been running into the proximal limb is diverted to the collateral vessels; column of blood trapped behind in the proximal narrowed segment may clot, drawing closer the walls of the vessel.

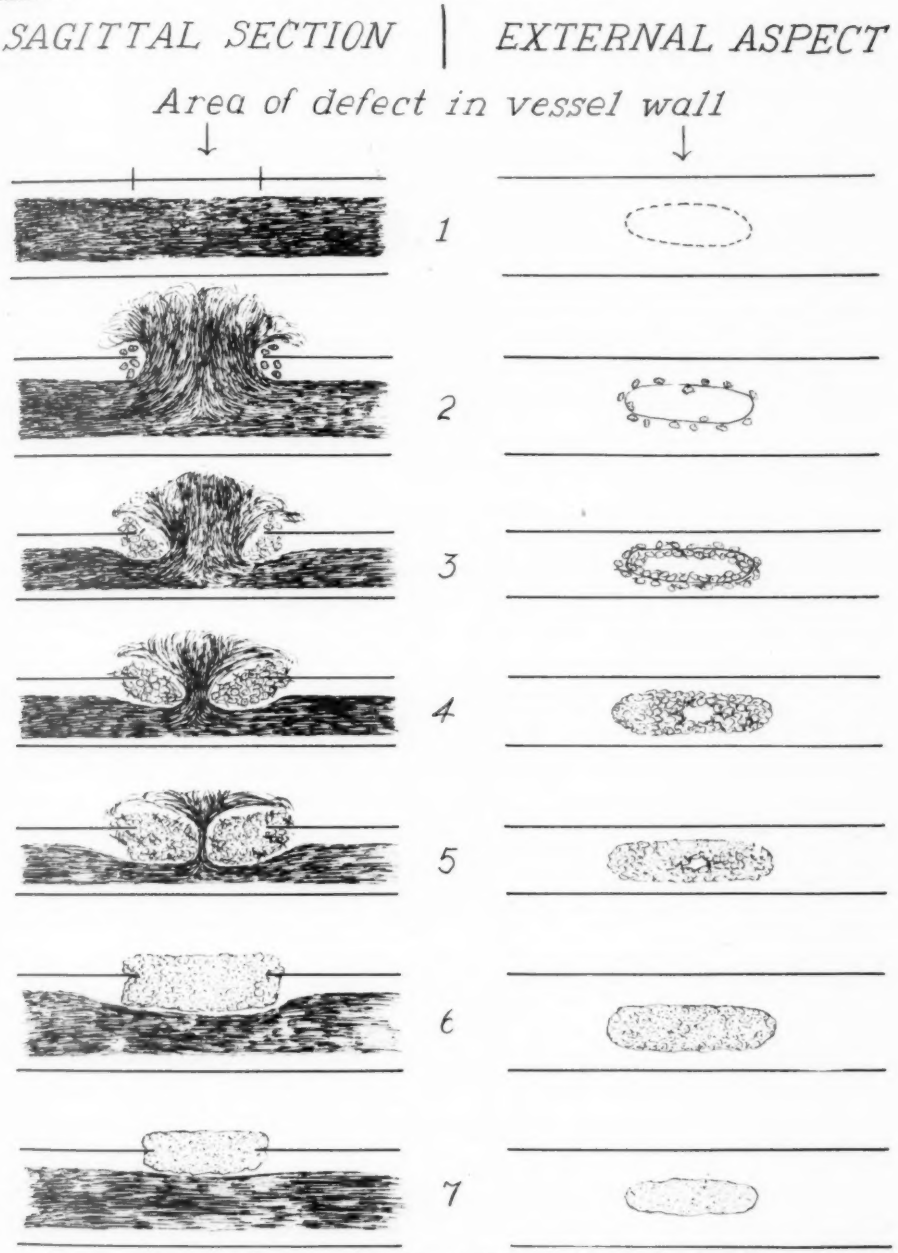


FIG. 6.—Diagrammatic Representation of Hemostasis in a Perforating Defect in a Thin-walled Vein.

(1) Oval defect in vessel wall.

(2) Escape of blood through opening; massing of platelets at edges.

(3) Diminution in intravascular pressure; partial collapse of vessel; reduction of lumen; increase in platelet massing.

(4) and (5) Reduction of opening because of increasing platelet and fibrin plug; diminution in volume of blood escaping from the orifice.

(6) Closure of the vascular defect by the platelet/fibrin plug, part of which is within and part outside the vessel. Cessation of bleeding; expansion of the lumen of the vessel.

(7) Contraction of the platelet/fibrin hemostatic plug.

but seldom to capillaries and veins. This is the reverse of thrombopenic purpura, a disease in which the disorder of hemostasis is manifested principally by hemorrhage from venules, veins and capillaries.

(b) Failure of spontaneous hemostasis may not necessarily follow a deficiency or absence of any one or even two of the factors named, provided the existing stresses are moderate and exerted chiefly on vessels not wholly dependent on those factors to check the flow of blood. For example, injuries to inelastic sclerotic vessels (in the aged) are seldom accompanied by much blood loss, if the vessel is a venule or vein, but of serious import if the injured vessel is an artery of large caliber.

(c) Most methods of securing hemostasis are attempts to duplicate, in one way or another, the principal steps of the natural mechanism of hemostasis, namely:

(1) *External compression,* by the use of dressings, packs, distensible bags and other devices.

(2) *Contraction and retraction of the vascular wall,* by using ligatures, clamps, forceps or certain drugs like epinephrine.

(3) *Formation of the hemostatic plug,* by supplying (blood transfusion) or aiding the body to produce prothrombin, fibrinogen, platelets or other constituents that it may lack.

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THORACIC SURGERY IN A HOSPITAL CENTER

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AND

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PART II

ABDOMINOTHORACIC INJURIES

Abdominothoracic injuries admitted to the Center have presented characteristics which set them apart as a group. Severe initial injury has been followed by a multiplicity of complex problems of rather constant origin. The right side has differed from the left although the course for each has been quite typical. They have required close correlation of thoracic and abdominal procedure.

Of 28 abdominothoracic injuries secondarily treated at the Center, 18 were on the right side and 10 on the left. Thoracic exploration had been done in 13; abdominal exploration in seven, and combined through the same or separate incisions in eight. After intrathoracic procedure, only six chests had been drained. The diaphragm had been almost routinely closed with interrupted silk. Subphrenic procedure had involved the spleen, intestines, kidney, liver and other viscera. Abdominal or flank drainage of the subphrenic area was limited to four on the right side.

On the right side, 18 cases were diversely distributed. Seven patients had empyema, with transdiaphragmatic bile fistulae. All were massive and had been repeatedly aspirated for fluid containing bile. Clinically, they had been only mildly toxic. None had progressed to constrictive pleuritis, necessitating decortication, if a bile fistula freely communicated with the space. All have responded well to closed and subsequent open dependent thoracic drainage. Two residual transthoracic biliary fistulae healed with diversion of the biliary stream to the exterior by radial incision of the diaphragm.

Suppuration above and below the diaphragm coexisted in four patients. Interposition of the diaphragm with separate thoracic and subphrenic drainage were extensive procedures, but uniformly successful. In two, spontaneous closure of fistulae had cut-off free flow of bile into the thorax. Suppurative constrictive pleuritis of clostridial origin followed, and had the only two decortications on the right side. One patient had severe hemorrhage from a suppurating liver defect which required pedicle muscle graft and thoracoplasty.

Subphrenic suppuration without thoracic involvement occurred in seven cases. It uniformly followed premature healing of drainage sites with reaccumulation of infected bile. All recovered with drainage across the diaphragm and obliterated pleural space. One recurrence was reoperated. Localized abscesses around intrahepatic foreign bodies have been rare. Secondary empyema followed such foreign body extraction and transpleural drainage in one case.

The situation on the left side was different. Suppuration was limited to

the thorax in six cases, to the subphrenic area in one, and combined in only three. Seven cases required decortication for suppurative constrictive pleuritis but only two acute empyemata were drained. Three diaphragmatic repairs and one splenectomy were done. Two subphrenic collections were drained and two were closed after instillation of penicillin. There were no deaths in any abdominothoracic cases.

Some points deserve emphasis. Infection as a uniform complication of abdominothoracic injuries has been associated rather constantly with insecure closure of the diaphragm and lack of thoracic and subphrenic drainage. Suppuration in these severe injuries has predisposed to severe illness.

On the right side, bile empyema, with a high incidence of *Clostridial* infection, has been common. They have done well on drainage and required few decortications. On the left, suppurative constrictive pleuritis necessitating decortication has predominated. No *Clostridia* have been observed. Diaphragmatic herniae and intrahepatic foreign bodies have not been as important as expected. The surgical problems in these cases have been complicated and required a diversity of methods. Adequate correlation has been often possible only with extensive procedures. Chronic biliary fistulae and suppuration may recur in many of these patients.

FOREIGN BODIES

Although foreign body removal has been the most frequent procedure in this study, its numerical prominence does not signify similar surgical importance. Incidental tissue damage and sequelae have generated more problems than the retention. They can be presented best as a separate entity but not always considered a separate problem.

Small bodies (less than 1.5 cm. in all diameters) have been associated with little tissue damage and few sequelae. As parenchymal bodies they have been well-tolerated and usually asymptomatic except in the heart. None have abscessed or bled. Some in the pleura have caused persistent hemothorax but empyema has followed only rarely.

Large bodies have often damaged tissue severely and implanted infected material. Retention of them must share with all other factors a fair responsibility for the high incidence of late sequelae. Fifteen (71 per cent) of 21 foreign bodies in or communicating with the pleural space were associated with late sequelae; clotting occurred in ten cases, and eight of these suppurated. Five had acute empyema. In the lung extensive surrounding reaction has generally cleared. Some have been surprisingly asymptomatic. Others have had irregular sputum, hemoptysis and unexplained pain. Eight abscesses formed around two fragments and in six tracts. Two of these also had interlobar empyema. The course of rib fragments has similarly depended on size and persistent defects.

One hundred and thirty-eight foreign bodies have been removed from the thorax; 98 as a primary elective procedure and 40 as an incident during surgery for other cause.

LUNGS AND PLEURA

Sixty-eight foreign bodies in the lungs were evenly divided between the two sides. Although most had recovered from a mild antecedent hemothorax some were removed and minor clotting cleaned-up at the same time. Accurate location has always preceded operation. It has been often possible to extract those near the thoracic wall by incision through an area of adhesions. In the more centrally placed, the lung usually has been free or only lightly adherent.

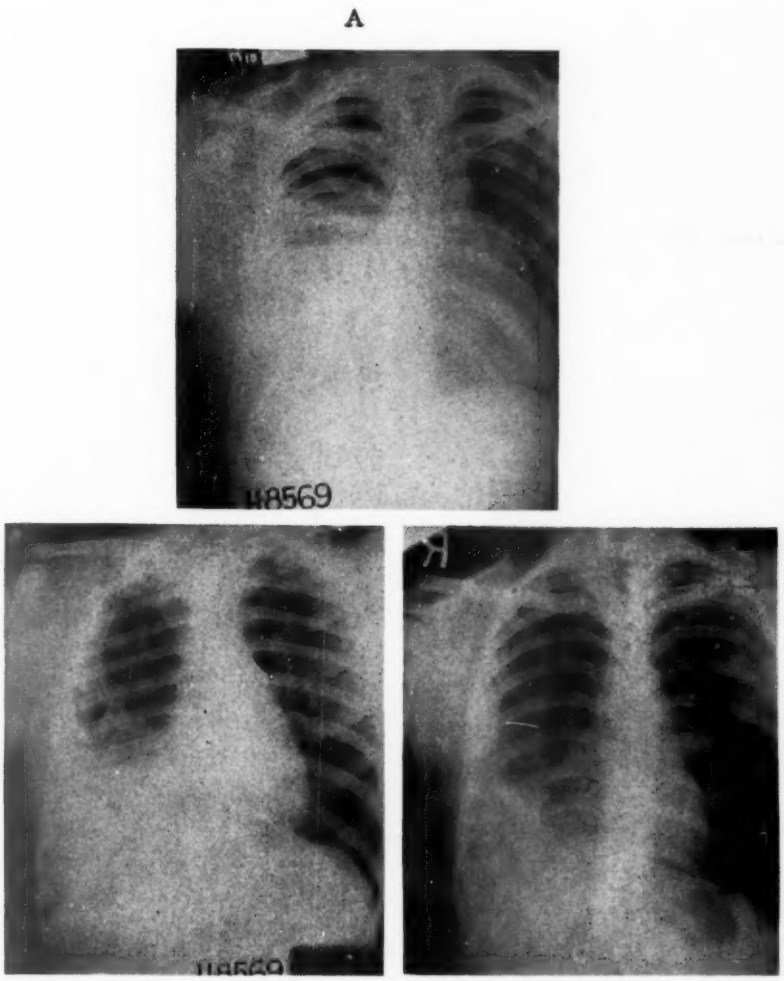
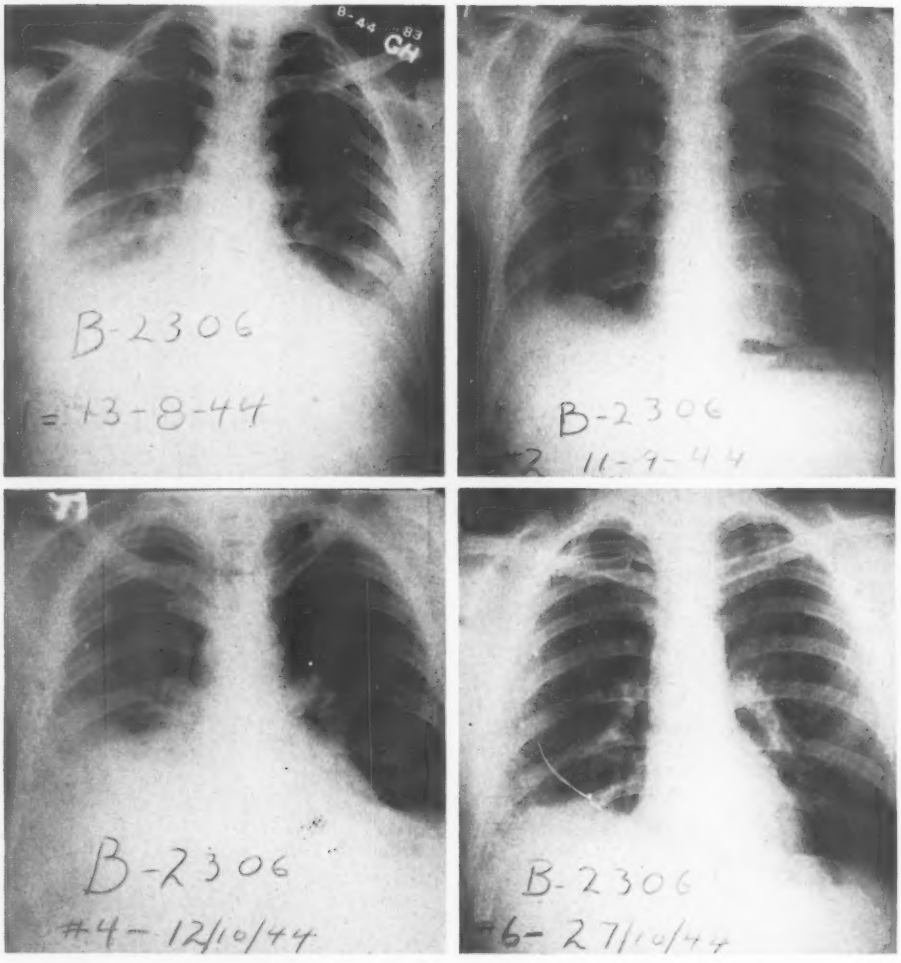


FIG. 7.—H-8569: Injured: August 6, 1944. Right abdominothoracic wound.
A. August 15, 1944. Right empyema, subphrenic abscess, thoracic wall fistula. (*Clostridia welchii*).
B. September 3, 1944. Result 16 days after open thoracic drainage and radial incision of diaphragm.
C. October 19, 1944. Result 62 days after operation.

To insure safety, the thorax has been opened widely except in a few near the fissures. The lung has been freely incised to allow visual extraction. The residual cavities have been treated by various methods. All have been thoroughly washed with saline and 10,000 units of penicillin instilled. An occasional large peripheral cavity entered through adhesions was drained by a small tube which was penicillin-irrigated during gradual withdrawal over 48

A B



C D

FIG. 8.—B-2306: Injured: July 14, 1944. Abdominothoracic wound, right.

A. August 13, 1944. Right empyema and subphrenic abscess with biliary thoracic fistula. (*Clostridia welchii*).

B. September 9, 1944. Result 27 days after drainage of right chest and subphrenic space.

C. October 12, 1944. Recurrent empyema and right subphrenic abscess.

D. October 20, 1944. Result 8 days after redrainage of right chest and radial incision of right diaphragm for subphrenic abscess.

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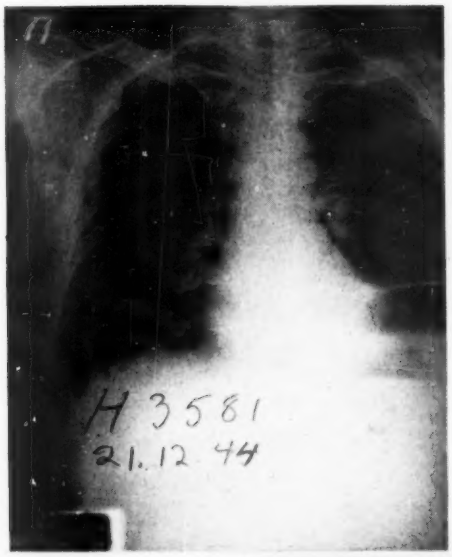

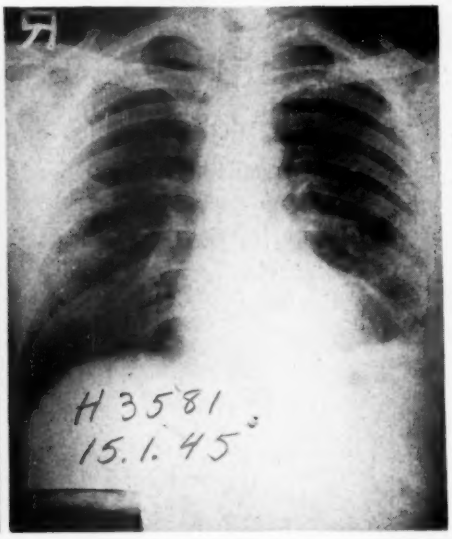

B C

FIG. 9.—H-3581: Injured: November 24, 1944. Left abdominothoracic wound. Repair of lacerated diaphragm at original operation.

A. December 21, 1944.

B. December 28, 1944. Diaphragmatic hernia left, with incarcerated stomach.

C. January 15, 1945. Result 12 days after splenectomy for lacerated spleen, with secondary hemorrhage and suppuration and repair of diaphragmatic defect.

hours. All others, with or without free opening of pleura, have been closed without drainage. Control of fistulae, hemorrhage and approximation of pleural edges has not been difficult with a few fine (No. 120) interrupted cotton sutures. In a few the wall was excised before closure if changes prevented ready collapse. Pleural spaces that were freely opened were drained generally for 48 hours by a single basal catheter after the insertion of penicillin. Bronchoscopy has been routine.

In spite of positive cultures in 62 per cent of these cases, no secondary empyema nor abscesses have occurred. All have had primary wound union, and were ready for rehabilitation in 21 postoperative days.

Only six of 21 metallic bodies removed from the pleural space have not been associated with clotting or suppuration. The elective extraction of these has been simple and without complications.

Forty foreign bodies removed as a part of other procedures have been either in the lung or pleura. Most important have been those lying in the apex of a fistula which prevented its closure and predisposed to suppurative constrictive pleuritis. Removal of 38 has been without complication. In two clean decortications, positive cultures around foreign bodies may have contributed to secondary empyema.

MEDIASTINUM

Ten foreign bodies have been removed from the mediastinum. They were asymptomatic and without complication. Four were removed extrapleurally and six transpleurally, with uneventful recovery. One patient with penetration of the lung and mediastinum developed a superior mediastinal and retropharyngeal suppuration, with a tracheo-esophageal fistula. He had respiratory obstruction in spite of a tracheotomy. Emergency enlargement of the tracheotomy opening, through which an endotracheal anesthesia had been administered, permitted the one instance of heroic surgery. Through bilateral cervical incisions joined in the midline at the suprasternal notch, the abscess was drained and the trachea separated from the esophagus after partial thyroidectomy. He completely recovered after tube-feeding for only ten days.

HEART AND GREAT VESSELS

Twenty foreign bodies directly involving the heart or great vessels represent 10 per cent of the total cases operated upon, but 20 per cent of the bodies electively removed. They were in the following locations:

a. Right auricular wall	3
b. Right ventricular wall	4
c. Right ventricular chamber	1
d. Left ventricular wall	2
e. Interventricular septum	1
f. Within the pericardium	3
g. Superior or inferior vena cava or innominate vein	3
h. Pulmonary arteries	3

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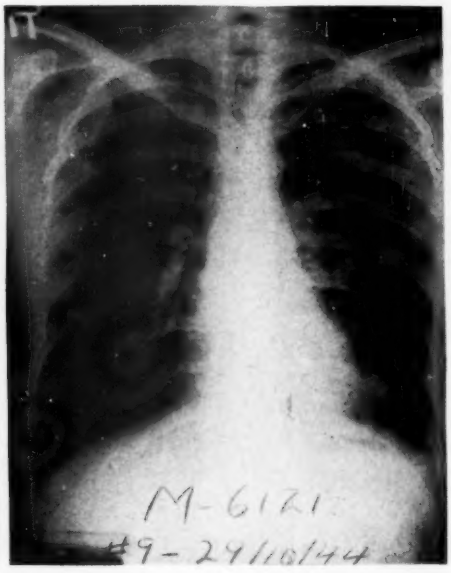

B C

FIG. 10.—M-6121: Injured: September 7, 1944. Penetrating wound left chest.

A. & B. October 18, 1944. Asymptomatic foreign body in periphery of left upper lobe, without reaction.

C. October 29, 1944. Result 10 days after operation.

All of these patients failed in the forward areas to react favorably to usually effective treatment for rather common hemothorax or hemopneumothorax. Fluid tended to persist. In about half, a correct diagnosis was made promptly by either clinical or roentgenologic criteria of hemopericardium. These improved immediately with aspiration. In the remainder, the picture was so masked that they went unrecognized until admitted to the U. K. Hospitals.

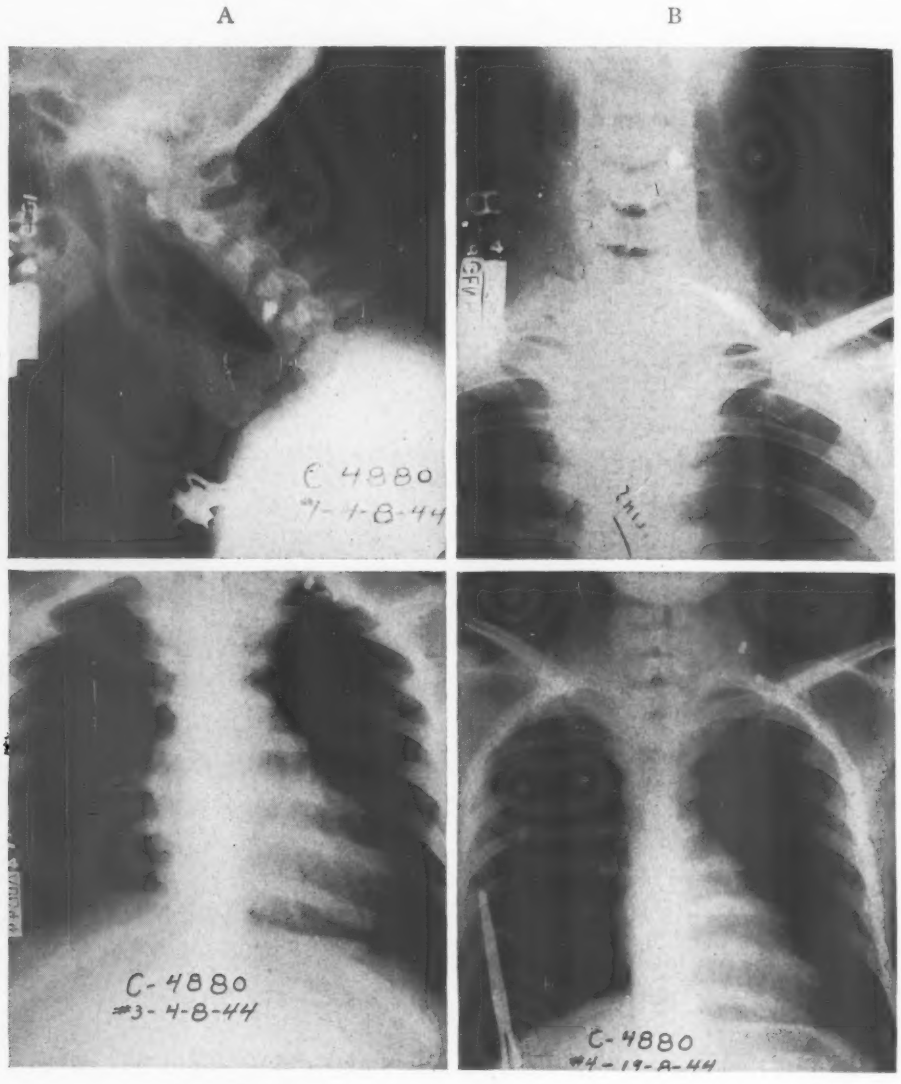

FIG. 11.—C-4880: Injured: July 30, 1944. Penetrating wound of neck left chest with tracheo-esophageal fistula.

A. August 4, 1944. Postpharyngeal abscess containing air;

B. & C. foreign body in neck; superior mediastinal abscess and subcutaneous emphysema.

D. August 19, 1944. Result 15 days after operation. The procedure is described in the text.

Findings in subsequent diagnosis have varied. Some have been practically asymptomatic, with inconstant, minor precordial pain. Syncopal attacks resembling coronary thrombosis or acute pericarditis have recurred and drawn attention to the heart, without adequate explanation. An enlarged cardiac outline or foreign body have been found on physical examination or in roentgenograms. Superposition due to oscillation with the heart has been typical. However, repeated roentgenograms have not shown many because of motion, small size or pleural exudates. Films with high power and short exposure, or fluoroscopy, have been frequently necessary to visualize and locate them accurately. Electrocardiographs, generally, have been abnormal and variously interpreted, with a predominance of pericarditis.

Cardiac bodies have been extracted through a left transpleural parasternal incision curved out over the 4th or 5th interspace. Mobilization of musculocutaneous flaps, with division or resection of costal cartilages, has been very satisfactory for exposure and closure. Sternal splitting, extrapleural and other incisions have been utilized less and only as necessary. Trap-door opening of pericardium has been hinged just anterior to the phrenic nerve. Several points of technic have proven of particular value. Adequate exposure of the apex has enhanced ease and safety of operation. The liberal intrapericardial application of procaine (5 per cent) before manipulation has prevented arrhythmia. Hammock sutures routinely placed underneath the foreign body in the cardiac wall, and often traversing a chamber, have steadied it during removal. They have prevented displacement into the heart, which often has been opened. Closure has been accomplished with little loss of blood by crossed-tension on them and a few interrupted sutures of cotton. Then the hammock sutures have been removed. This has been more satisfactory than apical and parallel mattress sutures and without discernible ill consequence.

An adhesive obliterative pericarditis had to be freed in every case in which the foreign body traversed the pericardial space. It has been drained into the pleural space by neglecting to close the inferior portion of the pericardial incision. Four partial pericardiectomies have been done for constrictive lesions. Opening of the left pleural space has been followed by closed drainage after pericardial and pleural instillation of 100,000 units of penicillin. Although eight (40 per cent) of the fragments have yielded positive cultures, secondary suppuration has not occurred in any case.

Foreign bodies in, or communicating with, the lumen of great vessels have been removed after control of the circulation by temporary ligatures to prevent hemorrhage and air embolism. The defect has been easily closed by interrupted cotton sutures except for one pulmonary artery branch ligation. Heparin has been used in only one case. One minor infarction followed suture of the pulmonary artery but improved rapidly. This has been the only adverse incident in six cases.

Roentgenograms showing early cardiac enlargement have returned to normal in 21 to 28 days. Electrocardiographs have not shown changes which

can be attributed to surgery. They have not regressed, but generally improved. No deaths and no significant postoperative complications accrued as the result of this work. The risk of one foreign body lying in the posterior auricular right wall did not warrant removal.

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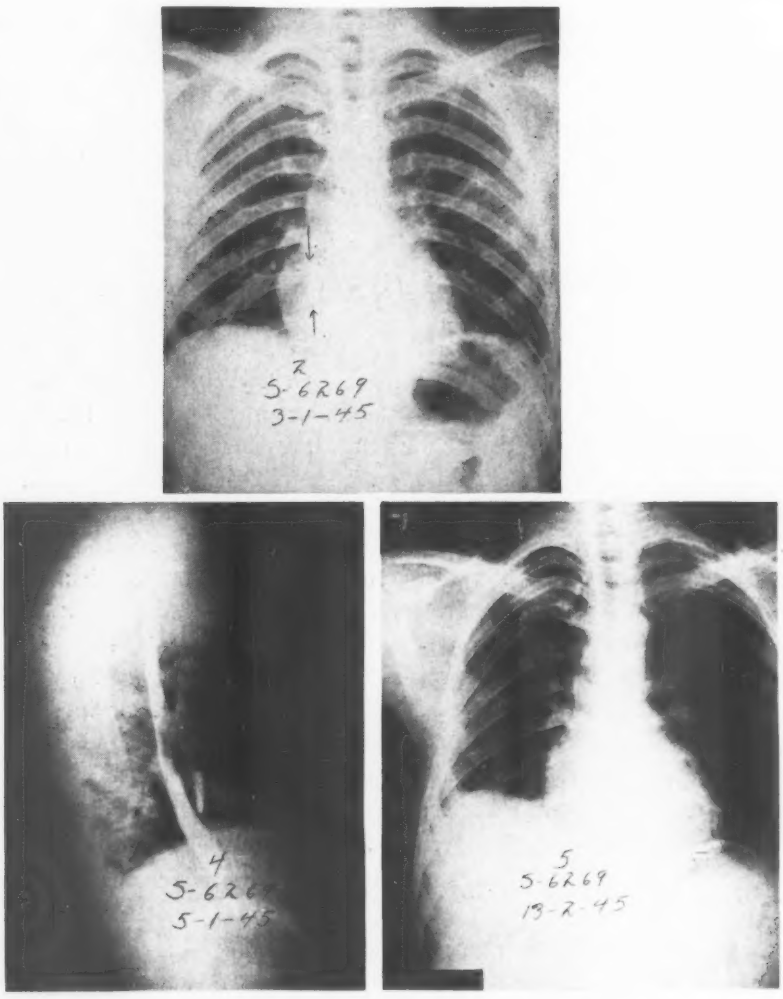


B C

FIG. 12.—S-6269: Injured: December 12, 1944. Gunshot wound of left chest. Left hemothorax treated by aspiration.

A. January 3, 1945.

B. January 5, 1945. Bullet in percardium.

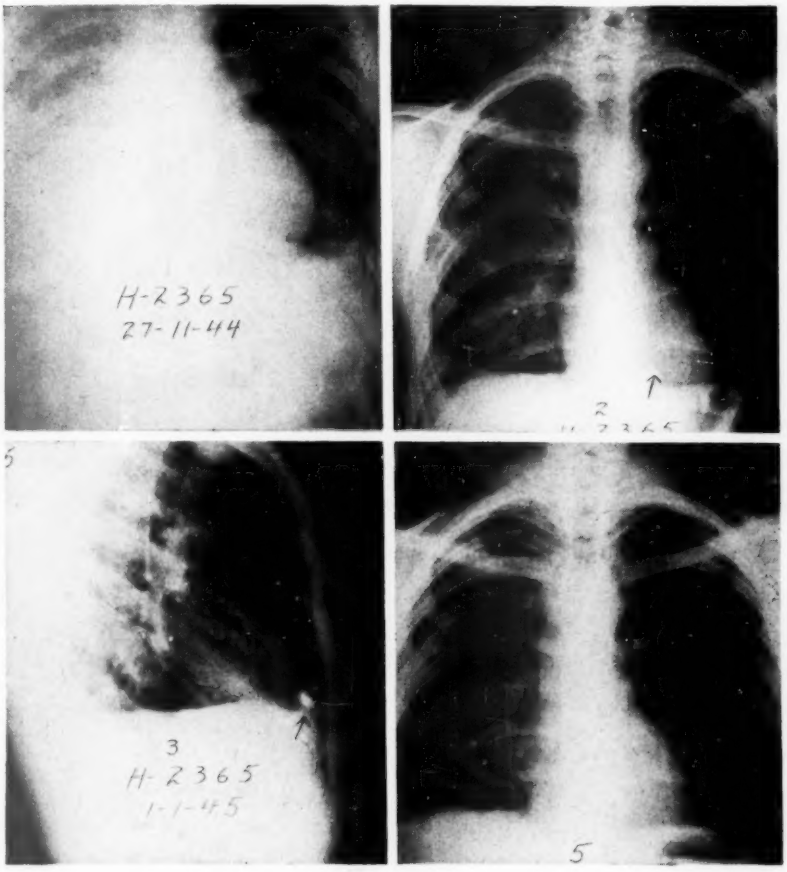
C. February 13, 1945. Result 28 days after operative removal and partial pericardectomy. (Culture of foreign body—gram-positive cocci).

All E. K. G.'s interpreted as indicative of percarditis. Returned to normal 35 days after operation.

Three unusual cases deserve special attention.

A shell fragment broke loose as an embolus from a right femoral arteriovenous fistula and, traversing the heart, lodged at the base of the right lower lobe. The artery was opened distal to the foreign body, which was extracted with a small hemostat and the branch ligated. The infarcted section, which had broken down, was shelled-out easily and the middle lobe was laid over this area. Immediate recovery was uneventful. Subsequent rapid cardiac dilatation secondary to emphysema, infarction and the fistula required closure of the

A B



C D

FIG. 13.—H-2365: Injured: November 22, 1944. Penetrating wound right chest and pericardium. Débridement and closure of wound with closed drainage at original operation.

A. November 27, 1944. Right hemothorax and hemopericardium.

B. & C. January 1, 1945. Foreign body in wall of right ventricle which projected into the ventricle-adhesive pericarditis.

D. February 13, 1945. Result 28 days after removal. An E. K. G. interpreted as indicative of pericarditis. After removal without pericardiectomy they returned to normal in 35 days.

fistula. After this was dissected and the continuity of the artery and vein established, the heart rapidly returned to normal size, without symptoms. Heparin, whiskey and sympathetic block were used and may have contributed to a rapid recovery.

Another shell fragment imbedded between the left lower lobe bronchus and the pulmonary artery projected into the latter, with a resultant hemothorax, which cleared. With mobilization of the artery the body was removed and

A

B C

FIG. 14.—J-1219: Injured: November 28, 1944. Shell fragment wound of abdomen. Exploratory celiotomy fragment not found.

A. November 28, 1944. Shell fragment not found at celiotomy on day of injury. Subsequent roentgenograms showed it had disappeared.

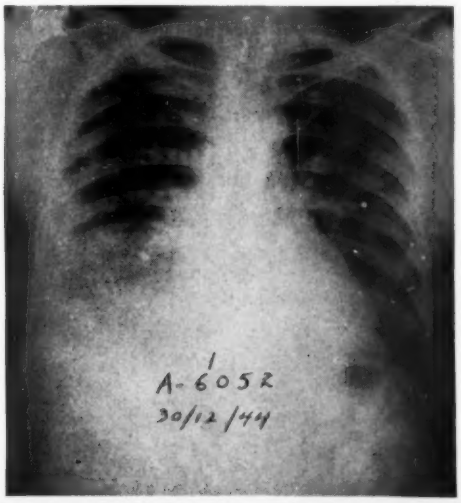
B. January 9, 1945. Shell fragment embolic to right ventricle.

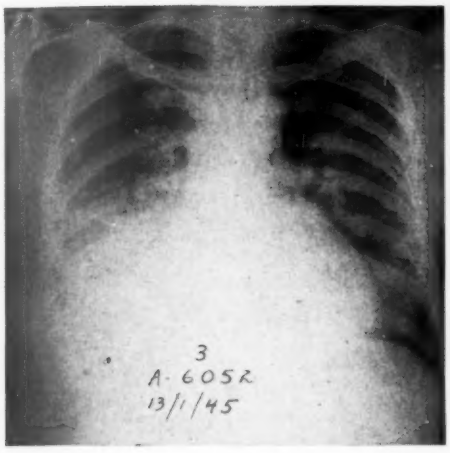
C. February 12, 1945. Result 21 days after removal from right ventricle.

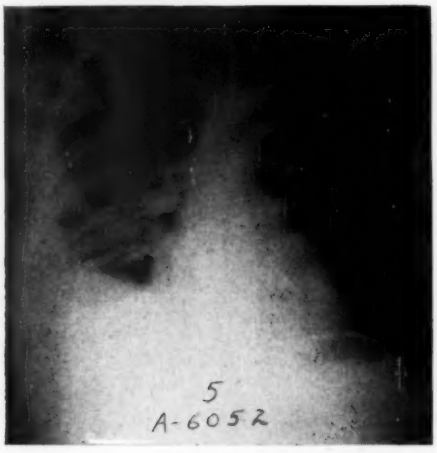
the vessel successfully sutured. Neither heparin nor whiskey were used. Recovery was uneventful in spite of minor infarction of the left lower lobe, which cleared completely.

After abdominal wounding, a shell fragment was visualized in the pelvis but subsequent examination disclosed it to be in the heart. It was removed

A







B C

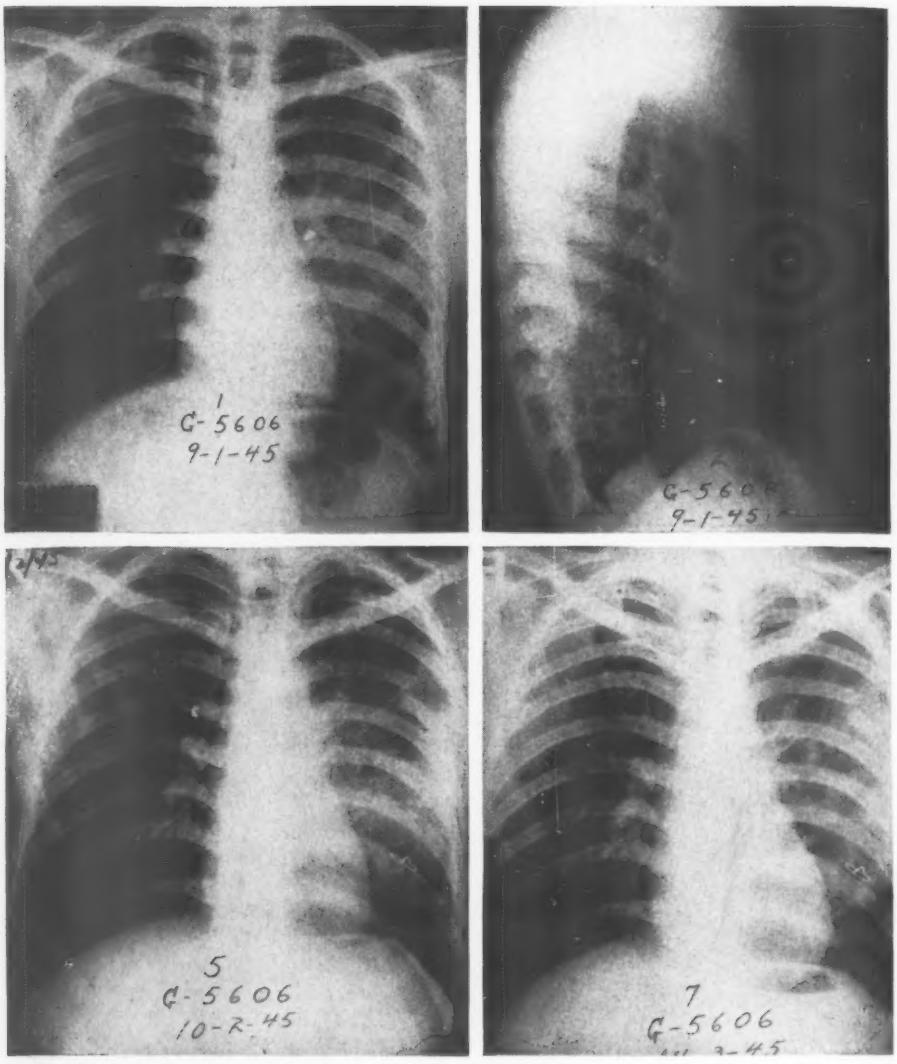
FIG. 15.—A-6052: Injured: December 12, 1944. Shell fragment wound of right femoral artery and vein.

A. December 30, 1944. Shell fragment embolic from right femoral vein into right pulmonary artery, with infarction of right lower lobe.

B. January 13, 1945. Result 11 days after removal of shell fragment, ligature of anterior portion of terminal artery and resection of sloughing infarcted right lower lobe. Note marked cardiac enlargement due to opening of large femoral arteriovenous fistula when shell fragment broke loose.

C. February 9, 1945. Marked regression in size of heart 16 days after repair of defect of artery and vein.

A B



C D

FIG. 16.—G-5606: Injured: December 17, 1944. Shell fragment wound left chest—retained foreign body. Débridement of wound and aspiration.

A. & B. January 9, 1945. Foreign body in left bronchus and pulmonary artery visualized through bronchoscope, with bleeding around it.

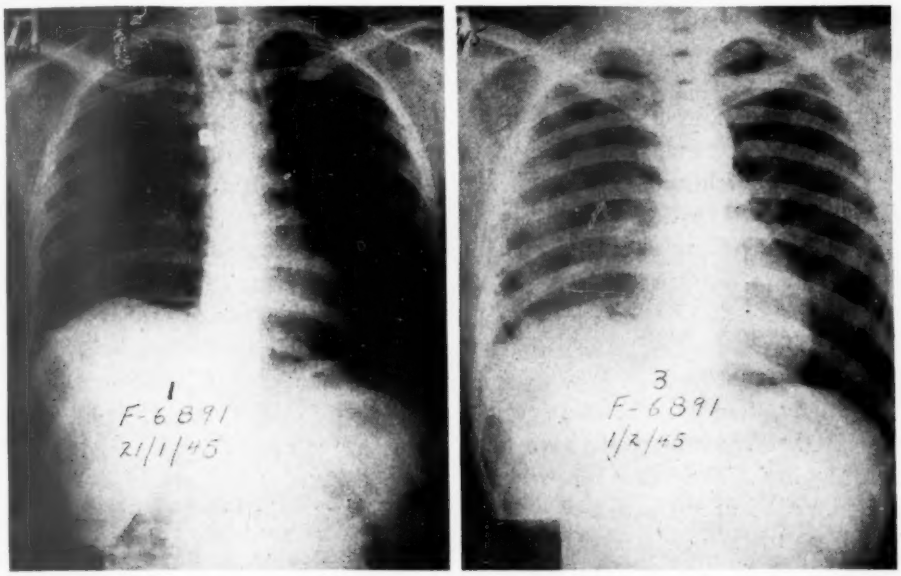
C. February 10, 1945. Result 22 days after left thoracotomy and removal, with suture of defects in pulmonary artery and bronchus.

D. March 14, 1945. Note clearing of infarction.

without incident from the right ventricular chamber. This is the single foreign body which did not exhibit an adhesive obliterative pericarditis.

MEDICAL THORACIC SECTION

A separate Medical Thoracic Section has performed a real service in supervising all general medical problems of diagnosis and treatment. The care of nutritional deficiencies, anemia and similar conditions, has been improved. The cardiologist and psychiatrist have lent valuable aid. The program of rehabilitation has been jointly shared. Individual instruction in breathing



A B

FIG. 17.—F-6801: Injured: December 4, 1944. Penetrating wound right chest.
A. January 21, 1945. Shell fragment in wall of superior vena cava projecting into its lumen.
B. February 1, 1945. Result three days after removal and suture of defect in superior vena cava. E. K. G. showed marked left axis deviation.

exercises has been started soon after admission. They have been continued immediately after operation. The most extensive procedures, including those on the heart, have not prevented mobility out of bed in 24 hours. In about seven days, when surgical attention was no longer required, the patients have been routinely transferred to the Medical Section. The spirit of these wards has cultivated confidence in the ability to get well. The rapid change from the incurable patient idea to soldier status has been invaluable in continuation of rehabilitation. As vital capacity has gradually increased, general exercises, competitive games, and other activities, have been introduced. Marked improvement in weight, strength, anemia, physical and mental health has closely followed. It is certain that this activity has contributed most to the ability to return to duty.

RECOMMENDATIONS FOR THE CARE OF THORACIC CASUALTIES

All casualties would benefit if they could be treated throughout all echelons by medical personnel specially trained in the involved field. The comparative shortage of qualified thoracic surgeons has accentuated the lack of such an ideal situation. However, past mistakes may be noted and avoided in less desirable plans which must be substituted. The belief by some that thoracic exploration in the forward area is a "push-over" is indicative of an attitude which is not amenable to correction by written instruction. Mere survival cannot be accepted as a satisfactory measure of efficiency of thoracic operation. The record shows that innumerable and excellent results have been achieved by qualified thoracic surgeons with a mortality that is approaching *nil*. Except for patients facing immediate disaster, every surgeon should be prepared to accept his results as the product of his work. If he will adhere closely to the principles and, when indicated, restrict his activity to that consistent with immediate preservation of life and safe transfer to care of qualified thoracic surgeons, the best interest of all will be served.

Special significance must be attached to common surgical problems when they occur in thoracic casualties because they initiate mechanisms which not only immediately threaten life but also profoundly influence future course. Hemorrhage, wounds and infection assume importance peculiar to the thorax.

Although methods of treatment must conform to accepted standard principles, they often must be of a special type to be applicable and efficient. It is evident that when methods have failed for any reason, principles have been compromised. The following procedures have proven to be some of the practical and efficient methods which permit rigid respect of principles which must remain as the sound basis of treatment.

TREATMENT IN THE FIELD

Few changes in field treatment are advisable.

Packing and occasional ligation usually suffice for control of hemorrhage. If it does not cease, it cannot be adequately treated without surgery and hospitalization. During this interval the continued use of blood and plasma is justified but should be supervised by a medical officer, since shock from disturbed thoracic mechanisms may require attention more urgently than blood loss.

First aid for cardiorespiratory imbalance has been quite satisfactory. Immediate closure of sucking or open wounds with occlusive dressings or packing should be continued. The erect or semi-erect positions, with the injured side dependent, contribute to efficiency of respiration. After wound occlusion, increasing distress must be attributed to a combination of progressive blood loss, tension and hemothorax. Aspiration should be sufficient to relieve acute distress. High negative pressures should not be sought since tension or hemorrhage may promptly recur. Surgery before hospitalization should be preserved for the rare extreme emergency. It is best displaced by intensive conservative therapy and evacuation to the greater facilities in hospitals.

TREATMENT IN FORWARD HOSPITALS

Many observers concur in the appraisal of thoracic surgery in the Forward Hospitals. Much has been exceptionally well done but too much has been done by others not trained in this field. Mistakes can be avoided in the future by simple measures upon which all agree.

Every patient should be carefully examined and clinically evaluated. The general course and the response to each therapeutic procedure must be carefully noted. Thoracic examination even with laboratory aids has been a poor substitute.

With careful examination the nonoperative cases may be readily separated for early disposition. Experience has shown that tangential nonpenetrating wounds of the thoracic wall and clean penetration by rifle bullets or small shell fragments are frequently followed by only minimal intrathoracic reaction. Hemorrhagic pneumonitis, atelectasis and hemothorax have recovered often without specific treatment. Although some minor cases may return to duty, any with moderate symptoms and all those entering or transversing the thorax, regardless of clinical status, must be evacuated to the rear.

The remaining patients cannot be evacuated immediately because of the possible or urgent necessity of therapy. This does not imply routine surgical approach. Institution of care should proceed with some routine plan since priority cannot be established easily for any one of a number of lethal conditions.

HEMORRHAGE

Continuing hemorrhage must be controlled. On the surface, or as a rapidly recurrent hemothorax, it should be easily recognized. Brisk bleeding from the thoracic wall has been more common than from the lung, where it usually ceases with pulmonary collapse. If packing or hemostatic ligatures fail, exploration under general anesthesia is indicated. The reaction to blood-loss replacement, oxygen and other measures in the absence of upset thoracic physiology is a good index of the necessity of operation.

CARDIORESPIRATORY FUNCTION

When patients fail to improve after control of hemorrhage, cardiorespiratory function must be investigated. Reëstablishment of it is not only essential to life but also intimately related to future results.

Respiratory exchange cannot be adequate without a competent air-way. The virtues of correct position, postural drainage, cough, oxygen, intercostal nerve block, strapping and tracheotomy, should supplement bronchoscopy, which cannot always reach the peripheral lesions.

Sucking wounds, open wounds, wounds with severe rib damage, and wounds with retained large foreign bodies, are incompatible with good results, and often life, if treated only with packing or dressing. All should be meticulously débrided and closed securely in anatomic layers, leaving the skin open if desirable. Needless sacrifice of any tissue, especially ribs and periostium,

should be avoided to permit easier and more secure closure. Wiring through drill holes is less painful than pericostal sutures. Unstable walls which embarrass respiration and early thoracic exercise and complicate secondary surgery can be prevented by attention to these details.

The continued presence of blood and air in the pleural space should not be tolerated. The most conservative measures which will keep the pleural space empty should be instituted immediately and persistently used to maintain this state. If this is done, the lung will expand to establish vital function at the same time that late complications are being reduced by obliteration of dead space, removal of fertile culture media and use of penicillin. At least 70 per cent of all patients with hemothorax, pneumothorax or hemopneumothorax will recover with such treatment.

A number will not exhibit progressive lung expansion or clinical improvement and clearing of roentgenograms. If the thorax is closed, recurrence must originate from defects persisting from initial injury. Methods which can establish stability and induce gradual intrapleural changes are needed. Closed drainage is essential. In recurrent pneumothorax with or without tension an air catheter through the second space anteriorly, or elsewhere, as necessary, has been quite satisfactory. It is more effective than aspiration or the flutter-valve in controlling expansion which favors healing of fistulae. Massive and recurrent hemopneumothorax has not done well with either aspiration or a single basal catheter. Poorly-placed tubes have become occluded by clotting, expanding lung or a rising diaphragm and, also, could not release air as long as fluid covered the tube. Under these circumstances a low basal tube for fluid should be used as a supplement to the air catheter. This tube should be larger, multiple-holed and inserted horizontally along the upper border of the costophrenic sinus. The use of two tubes has been justified by experience, and seems acceptable for theoretic reasons. As air and blood are drained from the pleural space, the relatively greater leakage of air from the lung will convert the hemopneumothorax to a pneumothorax, except for minimal residual sinus collection. Assured evacuation of air prevents tension and permits progressive expansion. Residual collections have been small and well-localized after the lower tube has ceased to function. Recurrent hemothorax can be drained by a single basal drainage tube. If pure blood rather than a thinning exudate is continuously obtained from the pleural space, the diagnosis of continuing hemorrhage requiring surgery must be entertained.

In using tubes, certain points are of importance. They should have multiple holes, be of adequate size and properly installed. A No. 16 F. catheter, inserted by a cannula just through the parietal pleura, has been satisfactory for air. A soft basal intercostal tube (1–1.5 cm.) has drained best when inserted horizontally, and fairly dependently, with regard for position of the patient, lung and diaphragm to prevent early shut-off. The rate of expansion can be controlled to promote healing of fistulae by increasing the depth of immersion in the drainage bottle. This should never be elevated. They should be retained until expansion obliterates the pleural space or until the system

ceases to work. Patency can be maintained without risk by irrigation with penicillin solution (250 units per cc.). Although retention beyond 48–72 hours should usually be unnecessary, penicillin has stretched this safe period to about seven days.

EXPLORATORY THORACOTOMY

More conservative measures should be abandoned in favor of exploration when definite reasons exist. Some gravely injured patients face disaster unless the conditions are promptly corrected. Arrest of hemorrhage, repair of chest wall, defects and closed drainage are the essential procedures. Many can be expected to come to secondary operation because primary surgery must be designed to relieve only the emergency. Other indications appear when conservative measures do not yield satisfactory progress. Although this surgery may be temporarily delayed, it should be done early to prevent serious late complications. Efforts should be directed to meticulous cleansing of the pleural space and sinus tracts; removal of devitalized tissue and foreign material, closure of fistula and plastic repair of residual pleural, pulmonary and other defects. After such exploration the lung should be completely expanded, the thorax drained with at least two closed tubes, and the bronchi cleared by bronchoscopy or suction. Local and parenteral use of penicillin should be routine.

ANESTHESIA

Proper anesthesia is of primary importance in any thoracic procedure. If cardiorespiratory function is deficient or if intrathoracic operation is contemplated, or a risk, only general anesthesia with endotracheal technic is permissible. Any failure to insure adequate control of respiration may lead to incomplete operation and poor results or death. Chances should not be taken with local or intravenous agents.

ABDOMINOTHORACIC INJURIES

Abdominothoracic injuries require routine early exploration. Thoracic approach has many advantages and can be supplemented by other incision, as necessary. The high incidence of late suppurative complications may be partially attributed to improper drainage and insecure closure of diaphragm. Imbrication with interrupted and nonabsorbable sutures is an excellent routine for diaphragmatic rents. Some large ones may require suture to the thoracic wall. The pleural space should always be drained by a basal tube at least. An air catheter may be added as necessary. The phrenic nerve should not be crushed. Liver damage must always be dependently drained through an adequate flank or abdominal incision. If transthoracic drainage is necessary, every effort must be made to separate the thorax from the subphrenic area. Left subphrenic drainage is rarely necessary. Foreign bodies in the liver requiring major additional incision for extraction should remain undisturbed. Others can be removed. Large liver lacerations can be effectively treated with penicillin-saturated gauze, muscle grafts or closure. These injuries will always

carry a high mortality but these simple measures may reduce the inordinately high rate of late sequelae which have been some of the most difficult problems encountered to date.

CARDIAC INJURIES

Cardiac and pericardial injuries which survive initial trauma usually present an hemothorax and hemopericardium. The latter may be unrecognized. These patients should not be operated upon with haste. Acute cardiac compression can be controlled often by subxiphoid aspiration. Unremitting hemorrhage requires emergency exploration and possible suture of the heart. Foreign bodies in the pericardium do not demand immediate pericardiotomy. They should rarely be removed early, except when the sac has been opened for other cause. Aspiration permits beneficial delay and recovery from the precarious state which cardiac trauma initiates. In the muscle they are best undisturbed unless necessary for the control of hemorrhage. Within the heart they should be disregarded. On exploration of any traumatized pericardium the virtues of 5 per cent procaine, adequate exposure, pleuropericardial and pleural drainage, must not be neglected.

Injury to great vessels usually is expressed as a rapidly recurrent hemothorax. After prompt control of bleeding, efforts must aim at repair of vessel walls rather than ligation. Foreign bodies in the walls can be removed and suture completed after adequate control of circulation by temporary and properly-placed hemostatic ligatures. Heparinization has not been necessary in a large group of such cases.

FOREIGN BODIES

Foreign bodies are usually not the concern of Forward Hospitals. When they are in the pleural space, they should be removed early. Operation for others may be delayed or be incident to exploration for other cause.

CHEMOTHERAPY

Chemotherapy has contributed greatly to the improved results in thoracic casualties. No comparative basis exists to permit expression of more than opinions. The oral use of sulfa-drugs has had no demonstrable ill effects, and may be continued. Insertion in wounds should be discontinued because it has often occasioned foreign body reactions without evident benefit.

Intrapleural penicillin appears to have been very useful. After each aspiration and exploratory thoracotomy, 40,000 units should be instilled. Results further justify the intramuscular use of 120,000 units daily for three to five days after operation of serious wounding.

EVACUATION

After emergency care has established stability, air evacuation to Thoracic Center holds the greatest promise. If for any reason evacuation must be slow, use of conservative measures, along the line, must be intensified. Emergency operation should be a rarity. At the onset of any indication for thoracic surgery, prompt transfer to a Center should be effected.

REAR HOSPITALS

Hospitals between the forward area and the Centers should, except in rare emergencies, confine their activity to the use of conservative measures. All medical officers should be alert to recognize poor progress or other indications for surgical therapy. While many general surgeons could do much of this work, the records do not substantiate this as the policy of choice. Until such time as the principles are more widely disseminated and regarded, the greatest good rests in transfer of these cases to the Thoracic Centers.

THORACIC CENTERS

The procedures, as outlined, have given good results in this Center. They should be interpreted neither as the only, nor necessarily the best, methods

TABLE IV

DISTRIBUTION—28 ABDOMINOTHORACIC INJURIES OPERATED UPON AT THORACIC CENTER

	Thoracic Center										Forward Area	
(A) Right side—18 cases	Operations						Cultures				Procedure	
	Number	Thoracic Drainage	Decortication	Subphrenic Drainage	Repair Diaphragm	Foreign Body: Removal	*Staph. aureus*	*Strept. hem.*	*Clostridia*	Others	Thoracic Drain	Subphrenic Drain
Complication												
I. Thoracic suppuration	7	7	0	2		1	4		5		3	2
II. Subphrenic suppuration	7			7		1	2	3	4		1	2
III. Combined thoracic and subphrenic suppuration	4	2	2	4	2				4		1	0
Total	18	9	2	13	2	2	6	3	13	0	5	4
(B) Left side—10 cases												
I. Thoracic suppuration	6	1	5			1	3	1		1	1	0
II. Subphrenic suppuration	1			1		1	1				0	0
III. Combined thoracic and subphrenic suppuration	3	1	2	2	3		2	1			0	0
Total	10	2	7	3	3	2	6	2	0	1	1	0

that can be applied. Further survey of all results will give a sound basis for final evaluation. They have significantly lowered morbidity. There have been no deaths in 200 consecutive operative cases reported in this paper.

SUMMARY

The observations on 300 patients treated in a Thoracic Center are reported.

Conservative measures have been quite effective in the early care of thoracic casualties. Proper use of minimal procedures in sucking wounds, hemorrhage and shock, has averted immediate death and permitted complete recovery in many patients. A small number have required emergency operation.

Hemothorax, pneumothorax or hemopneumothorax have persisted frequently, and required further therapy. At least 70 per cent of them have recovered with repeated aspiration and chemotherapy. In the others, diverse

circumstances have led to progression. The failure to obtain and maintain early and maximal lung expansion has been associated with persistence, clotting and infection. Neglect of the implications and details of surgical care of extensive sucking wounds, bronchopleural fistulae and retained foreign bodies have aggravated the situation. Acute empyema, multiloculated hemothorax and simple or suppurative constrictive pleuritis have resulted. Decortication has been more widely needed than simple drainage. It is a formidable procedure but has reduced morbidity and carried no mortality.

Abdominothoracic injuries have had a high incidence of late complications. These have been universally suppurative and can be traced, in part, to improper thoracic and subphrenic drainage and insecure closure of the diaphragm. A

TABLE V

DISTRIBUTION OF ORGANISMS IN 200 OPERATIVE CASES

Diagnosis	*Staph. aur.*	*Strept. hem.*	*Clostridia*	Other	Total Cases	Total Positive Cultures	Comment
1. Acute empyema.....	5	6	4	6	14	14	
2. Constrictive pleuritis (simple).....	3	2	1	4	29	10 25%	Five positive cultures around foreign bodies
3. Constrictive pleuritis (suppurative).....	10	8	4	8	39	39	
4. Abdominothoracic injuries	12	5	13	1	28	28	All 13 *clostridial* cultures obtained from right-sided lesions
5. Foreign bodies (lung, pleura, med.).....	15	16	9	20	78	48 62%	
6. Foreign bodies (heart)...	4	4	0	0	20	8 40%	Around foreign bodies and from pericardium

multiplicity of extensive procedures have been required to cure these patients. Any success has been related to the possibility of repair or interposition of the diaphragm to separate the thoracic and abdominal components and permit individual treatment of each.

Foreign bodies have not been difficult. The majority have been asymptomatic and removed empirically by reason of size or location. Any tendency to induce late parenchymal changes has not been observed in a period which has been necessarily short. Elective operation for these have entailed neither mortality nor morbidity.

Some foreign bodies have been definitely associated with sequelae. Those in the pleura predisposed to empyema. Large irregular fragments have been frequently followed by fistulae, abscesses and delayed suppuration. All have been routinely removed without ill effect during operation for other cause.

The safety of surgical removal of foreign bodies from the heart and great vessels is established. This reported series of 20 has been increased to 30 successful operations, without serious complication and with no mortality.

Penicillin appears to be a most efficient agent. Its action is at least a plausible explanation of the results in the presence of so much suppuration.

A qualified anesthetist has been invaluable. Without gas, oxygen and

ether anesthesia, with endotracheal technic, and close supervision of the allied problems of circulation and respiration, much of this work would not have been possible. Routine postoperative bronchoscopy has yielded excellent results. Delegation of this to the anesthetist has been found highly satisfactory.

The rehabilitation of all thoracic patients has been most effective when total mobility has been obtained early.

Concentration in the hands of trained personnel has improved the treatment of thoracic casualties. In 200 consecutive cases definitive surgery has remarkably reduced morbidity and incurred no mortality. The greatest portion of improvement in results must be credited to the type of patient. He has been a young, previously healthy individual who has been able to face surgery with a minimum of risk.

CONCLUSIONS

The therapeutic problems of thoracic injuries fall into two basic groups: The first demand immediate attention to save life. They are concerned with the control of hemorrhage and the reëstablishment of cardiorespiratory function. The second does not threaten life immediately, and some delay in treatment is permissible. They involve the early maximal restoration of normal anatomic and physiologic relationships. Operative and nonoperative measures are useful in both groups, but they are not mutually interchangeable. Conservative measures should be pushed to the limit when they can suffice. When they fail or are unsuitable, operative approach is indicated. Success will be greatest when familiarity with, and regard for, principles governs the application of methods. Since this has not been uniform, a wider dissemination of the principles and possibilities of this field of surgery is needed.

The American soldier has been the finest patient in the world. The manner in which he has borne all his misfortune has kindled a sense of pride which has made the care of him a privilege. It is good to be an American.

Note: The activities of recent months has increased the series to 314 consecutive operative cases. The breakdown of these conforms closely to the figures detailed in this report. No deaths have occurred.

THE MODERN TECHNIC OF THE LE FORT OPERATION

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THE TREATMENT of a third-degree prolapse of the uterus is still a problem. The choice of the operation depends in a large measure on the condition of the uterosacral ligaments, the size of the uterus, the age of the patient, and whether matrimonial relationship is desired.

Of the several possible procedures the so-called modified Le Fort operation is the subject of the present communication.

The development of this operation dates from 1823, when Gérardin (Metz) had the original idea of resecting the lower portion of the anterior and posterior vaginal mucosa and then uniting the denuded portions to cure a third-degree uterine prolapse. But he never undertook the operation. Neugebauer (Warschau), in 1876, operated and published a case of uterine prolapse, according to Gérardin's method, though he resected a higher portion of the vaginal mucosa than Gérardin proposed. He gave the operation the name "elytrorrhaphia or colporrhaphia mediana" and reported, in 1881, 11 cases. Spiegelberg (Breslau), in 1872, used the same technic and Le Fort (Paris), in 1876, recommended this method for the treatment of uterine prolapse. The procedure is known in this country as the "Le Fort" operation and in the German literature as the "Neugebauer-Le Fort" operation. The first three cases operated upon by this method in the United States were reported 1881 by Berlin.

Many surgeons have used this procedure. The results, however, of the original Le Fort operation were not satisfactory and recurrences occurred. The plain resection of two symmetrical rectangular pieces of the anterior and posterior vaginal mucosa and the connection of the denuded areas proved insufficient. Many modifications (Adair and Phaneuf) were used in order to improve the results and to prevent recurrences. Most leading textbooks mention the operation but there are useful technical details not included in their description.

The causes of the recurrences have been almost universally the same: (1) The resected vaginal flaps were too small and consequently the lateral canals were too wide. (2) The approximated surfaces did not heal and partial separation occurred.

The numerous improvements of the operation result in the following technic, the main idea of which is a combination of four procedures: (1) Closure of a wide central portion of the vagina. (2) Formation of a suitable fascial support for the cystocele, the rectocele and the prolapsed uterus. (3) Formation of the inverted U-shaped canal. (4) Repair of the pelvic floor.

In the modern technic the resected flaps of the anterior and posterior vaginal mucosa are large and their shape is completely different the one from the other. The enlargement of the denuded area makes the diameter of the

U-shaped canal smaller.[9] The difference in the shape renders it possible to continue immediately with the plastic of the pelvic floor, which is a very important part of the operation.[31]

OPERATIVE TECHNIC

Three points should be marked as the limits for the incision of the anterior vaginal mucosa (Fig. 1). Point 1 is in the midline, half a centimeter below the external urinary meatus. Points 2 and 3 form the end-points of the anterior transverse incision which is about three centimeters above the cervical opening.

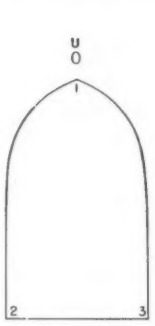

FIG. 1

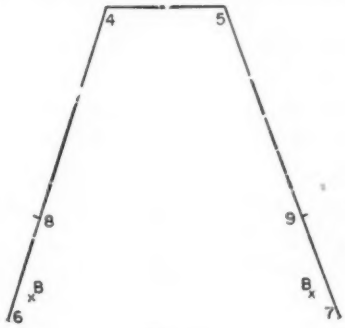

FIG. 2

FIG. 1.—Incision of the anterior vaginal mucosa. U is the external urinary meatus. Point 1 is half a centimeter below U. The transverse incision between Point 2 and Point 3 is three centimeters above the external uterine orifice.

FIG. 2.—Incision of the posterior vaginal mucosa. The transverse incision between Point 4 and Point 5 is three centimeters behind the external uterine orifice. Points 6 and 7 are at the border of the vaginal mucosa and the skin, close to the opening (B) of the Bartholin's glands.

The three points of the anterior flap should not be connected by straight cuts to form a triangle. It is better to make three-quarters of the lateral incisions parallel to the long axis of the uterus and the last quarter in a slight bow to the Point 1 below the urethra (Fig. 1). The resulting shape of the flap is frequently compared with a Gothic window or a snowshoe.[1] This flap of the anterior vaginal wall should be removed in one piece at once.

The shape of the resected portion of the posterior vaginal mucosa is completely different from the resected flap of the anterior vaginal mucosa. Four points have to be marked. Points 4 and 5 (Fig. 2) are the end-points of the transverse incision of the posterior vaginal mucosa, which is about three centimeters distant from the cervical opening. Points 6 and 7 (Fig. 2) are on the skin close to the opening of the Bartholin's glands.

The lateral cuts connect the Points 4 with 6, and 5 with 7, and give the posterior flap a trapecoid-shape (Fig. 2).

The idea of the different shape of the anterior and posterior flap is, that in forming the inverted U-shaped canal the Point 1 of the anterior incision (Fig. 1) will meet *the Point 8 as well as Point 9* (Fig. 2) of the posterior incision in the midline. From this point, where the Points 1, 8 and 9 meet, runs

the balance of the posterior incision, Points 8 to 6 and 9 to 7, to the skin (Fig. 2). This part of the incision corresponds exactly with the usual angular incision made in the routine colpoperrineorrhaphy. The advantage is, that, first, all unnecessary vaginal mucosa is removed; and, second, that the deep portions of the muscles can be reached to build a sufficiently supporting perineal floor. The end-points of the incisions at the skin, 6 and 7 (Fig. 2), can be connected by a slight bow, as used in the ordinary posterior plastic and, finally, the entire posterior flap is removed.

TECHNICAL DETAILS

In performing the transverse incisions near the cervix between Points 2 and 3 (Fig. 1), and between Points 4 and 5 (Fig. 2), care must be taken not to be too close to the external uterine orifice, otherwise the formation of the transverse canal below the cervix is impossible because the inverted vaginal mucosa would be too tight over the cervix.

The suturing of the vaginal edges in order to form the inverted U-shaped canal is one of the most important steps of the operation. A few rules for the canal sutures should be observed: (1) Only interrupted chromic catgut sutures, Nos. 1 or 2, should be used. (2) All knots must be on the inside of the newly-formed U-shaped canal, in other words, on the intact vaginal mucosa and not in the denuded area. This is necessary to unite the new edges of the vaginal mucosa by so-called inverted stitches. That means that the needle has to go first through the *posterior* vaginal mucosa *from the intact surface to the denuded area* and *then* through the anterior vaginal wall from the denuded area to the intact surface (Fig. 3). If not done in this way the intact tissue of the vagina would be brought together instead of the newly-formed wound edges and an exact healing would be impossible.

The direction in which the needle is passed through the vaginal mucosa is important in order to avoid a very disturbing tangling of the sutures. Figure 3 shows how to overcome this trouble. It is advisable in applying the sutures that the assistant at the respective side takes the end of the ligature in his hand before the needle passes the posterior wall and keeps the end of the ligature in his hand until the anterior vaginal mucosa is transfixed. These technical details help to avoid tangling of the sutures and allow an exact adaptation of the wound edges. In starting on the posterior wall, backhand stitches can be avoided and the technic will become much clearer and more exact.

In forming the U-shaped canal, the perivesical and perirectal connective tissue is approximated. Dead spaces and small hematomas, which cause failure in healing must be avoided. This is accomplished by use of No. 00 chromic catgut sutures, applied in an anteroposterior direction, passing first the perivesical and then the perirectal fascia. They should not be tied before a series of four to five sutures have been inserted. These stitches plicate the excessive tissue of the cystocele and rectocele.[7] After a few canal-forming stitches through the vaginal wall another series of middle stitches should be applied.

After the whole canal has been formed, the entire edge of the anterior vaginal wall has been used up and Point 1 (Fig. 1) of the anterior incision will be forced to meet Points 8 and 9 (Fig. 2) of the posterior incision in the

midline. This is the vertex of the angle formed by the balance of the posterior incision, which is used for the following colpoperineorrhaphy. The flap of the posterior wall which is still present is now removed by a transverse cut which connects the Points 6 and 7 (Fig. 2). Instead of the transverse cut an angular excision of the perineum can be substituted, which allows a better muscle plastic of the perineorrhaphy.

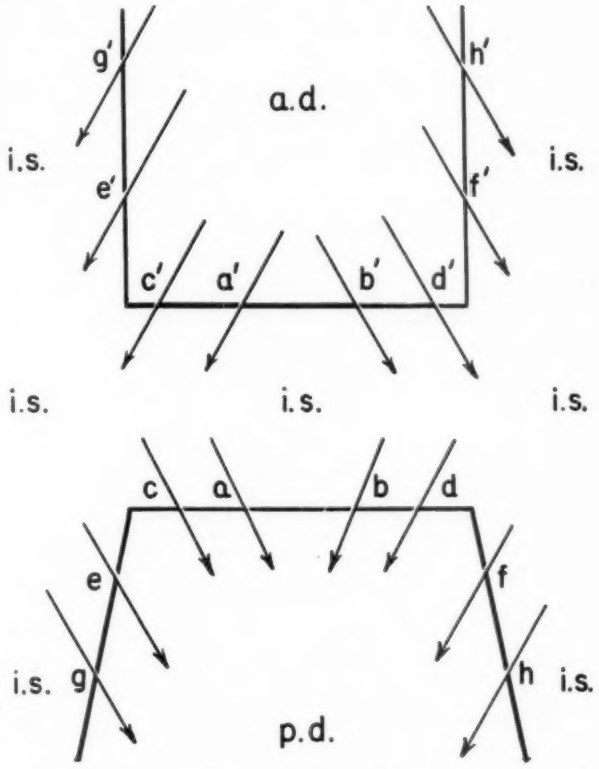

FIG. 3.—Direction of the canal-forming stitches aa', bb', cc' and so on. The needle has to pass first the *posterior* wall from the intact surface (i.s.) to the posterior denuded area (p.d.), and then the anterior mucosa from the anterior denuded area (a.d.) to the intact surface (i.s.). In this way the knots of the interrupted stitches will be on the intact surface and not in the denuded area.

CASE REPORTS

Case 1.—Mrs. H. D., age 60, has had four children. She complained of having a mass coming out of the vagina, causing severe difficulties in walking and sitting.

The vaginal examination revealed a mass as large as a man's fist, protruded from the vulva and lying between the thighs. The mass was covered by the inverted vaginal walls which were firm and dry. At the lower part of the mass was the cervix with the external os. No erosion or ulceration was present. The very small uterus was palpable between the vaginal walls. *Diagnosis:* Third-degree prolapse of the uterus and the vagina.

Operation.—The modified Le Fort operation was performed as described above.

The postoperative course was uneventful, and patient left the hospital on the 17th day. The examination on discharge showed a very good result.

Follow-up examination two years after the operation has shown an excellent result.

No bulging on bearing-down could be detected. Patient felt perfectly well and was free of complaints.

Case 2.—Mrs. J. S., age 66, has had three children. She complained of dragging pain in the back and pelvis which became worse when walking. She had the feeling that a mass comes out of the vagina, causing severe difficulties in walking and sitting.

The vaginal examination revealed a mass nearly as large as a fist protruded from the vulva and lying between the thighs. It was covered by the inverted vaginal walls which were firm and dry. At the lower end of the mass was the cervix with the external os. The fundus of the very small uterus was palpable between the vaginal walls. *Diagnosis:* Third-degree prolapse of the uterus and vagina.

Operation.—The modified Le Fort operation was performed as described.

The postoperative course was uneventful, and patient left the hospital on the 15th day.

Examination on discharge showed a very good result. There was a slight discharge from the openings of the inverted U-shaped canal, due to the degeneration of the vaginal catgut sutures.

Follow-up examination after two years has shown an excellent result. Patient felt perfectly well and was free of complaints.

Case 3.—Mrs. C. G., age 65, has had two children. A supravaginal hysterectomy was performed 20 years ago. Patient complained of dragging pain in the back and pelvis which became worse when walking. She had the feeling that a mass comes out of the vaginal opening which made her unable to sit or walk. She wore a ring pessary for many years, which had to be removed because of local irritation.

Vaginal examination revealed a mass as large as a man's fist, protruded from the vulva and lying between the thighs. It was covered by the inverted vaginal walls which were firm and dry. There was no uterus palpable between the vaginal walls but there was a very small cervix on the lower end of the mass. *Diagnosis:* Complete prolapse of the vagina following abdominal hysterectomy.

Operation.—The Le Fort operation was performed in the modification as described above.

The postoperative course was uneventful, and patient left the hospital on the 14th day.

Examination on discharge showed a very good result. There was a slight discharge from the opening of the inverted U-shaped canal, due to the degeneration of the vaginal catgut suture. Irrigation through the U-shaped canal could easily be performed.

Follow-up examination after two years has shown an excellent result. No bulging on severe bearing-down could be detected. Patient felt perfectly well and was free of complaints. Bladder function and bowel movement normal.

Case 4.—Mrs. C. M., age 71, had had three normal deliveries. She complained of dragging pain in the back and pelvis and the feeling that a mass is coming out of the vagina causing severe difficulties in walking and sitting.

The vaginal examination revealed a mass as large as a fist protruded from the vulva and lying between the thighs. It was covered by the inverted vaginal wall which was firm and dry. At the lower part of the mass the cervix could be recognized by the opening in the center. The entire very small atrophic uterus was palpable between the vaginal walls. *Diagnosis:* Third-degree prolapse of the uterus, huge cystocele and rectocele.

Operation.—The Le Fort operation was performed in the modification as described above.

The postoperative course was uneventful, and patient left the hospital on the 17th day.

Examination on discharge showed a perfect healing. A slight discharge from the canals could be removed by irrigation of the U-shaped canal.

Follow-up examination two years after the operation has shown an excellent result. No bulging on bearing-down could be detected. Patient felt perfectly well and was free of complaints.

Case 5.—Mrs. J. G., age 51, has had two children. She complained of having a mass coming out of the vagina, causing severe difficulties in walking and sitting. The vaginal examination revealed a mass as large as a man's fist protruded from the vulva. After

replacing the mass it was expelled on slight bearing-down. At the lower part of the mass was the cervix with the external os, the fundus of the uterus was palpable between the vaginal walls. *Diagnosis:* Third-degree prolapse of the uterus, cystocele and rectocele.

Operation.—The modified Le Fort operation was performed as described above.

The postoperative course was uneventful, and patient left the hospital on the 17th day.

Examination on discharge showed a very good result. There was a slight discharge which could be removed by irrigation through the U-shaped canal.

Recently, I reëxamined the patient. She has no complaints and feels perfectly well. No bulging on bearing-down could be seen.

DISCUSSION.—In the Cases 1, 2 and 4 the choice of the modified Le Fort operation was determined by the age of the patients (60–71), and that marital relations were no longer of importance. The youngest of this series, (Case 5) was 51 years of age. She was a widow, had a very small uterus and a complete relaxation of the uterosacral ligaments. Her general condition was not very good and, therefore, we decided to perform the Le Fort operation in the above described modified technic.

In Case 3 the choice of the modified Le Fort operation was easy. The absence of the uterus excluded consideration of hysterectomy as well as the interposition operation. There could be no better procedure for this case than the modified Le Fort operation.

A definite advantage of the operation is that there is practically no operative risk. The technic is not difficult, though it needs a certain skill to observe the mentioned technical details.

In favor of the operation is also the fact that the greater part of the entire procedure can be performed without any anesthesia. This may seem unbelievable, but experience has shown that the incisions and the removal of the anterior vaginal flap is completely painless even without local anesthesia.[31, 32] The posterior vaginal wall can also be removed without pain by careful separation, especially in the region close to the cul-de-sac of Douglas. The perineorrhaphy, of course, needs local anesthesia. Considering that the operation is performed mostly on aged patients, the advantage of performing the largest part of the whole procedure without anesthesia cannot be overlooked.

In the presented cases (1, 3, 4 and 5), I performed the separation of the anterior vaginal flap without any anesthesia, and the patients did not complain of pain. The separation of the posterior flap was also done without anesthesia until the region of the cul-de-sac of Douglas was reached. In the Cases 1, 3 and 5 I could continue until the entire U-shaped canal was formed. Before the last stitches of the U-canal are applied I start routinely with the infiltration of the perineum and the lowest part of the labia majora. In Case 4 I had to infiltrate the posterior vaginal wall in the region close to the cul-de-sac of Douglas. Case 2 was done under general anesthesia because the highly nervous patient desired to be under anesthesia before entering the operating room.

I do not feel that the possibility of a later development of a carcinoma of the uterus should be considered as a contraindication to this valuable operation, because irradiation and operative treatment is still always possible and the open U-shaped canal would reveal any suspicious discharge or hemorrhage at any time subsequently. Moreover, the incidence of uterine carcinoma in women with atrophic uteri is indeed rare.[1]

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COMPOUND INJURIES OF THE KNEE JOINT*

STUDY I—TREATMENT OF NONINFECTED KNEE JOINTS

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DURING THE TWO AND ONE-HALF YEARS in which the armed forces were engaged in active warfare, first in the Mediterranean Theater and later in the European Theater, many well-crystallized ideas about the surgical management of the wounded were developed. The program of early reparative surgery, as envisioned by Colonel E. D. Churchill, is, without doubt, one of the major contributions to come from the present conflict.

The surgery of wounds of the knee joint is an outstanding example of a field where clear, concise ideas of the proper type of surgical care have evolved. The early care of these penetrating and perforating injuries is now well-standardized. The joint must be opened widely and explored in order to remove all destroyed and devitalized cartilage and bone. The synovium is then closed, and penicillin is instilled into the joint. The skin is left open in the Forward Hospitals.

The Office of the Surgeon-General has recognized the need for early, thorough exploration of compound injuries of the knee. Technical Bulletin No. 147, published in March, 1945, states: "The wound of the soft-part is excised and the bone and cartilage damage assessed through incisions that provide complete exposure. Comminuted fragments of bone and cartilage are removed from the joint and a careful search made for foreign material." Thompson, Cassebaum, and Stewart recorded the experiences of an Evacuation Hospital in treating war wounds of the knee. Their observations were based on 172 penetrating injuries of the knee, 131 of which were subjected to formal, exploratory arthrotomy. We received many of these patients and know that the results were excellent.

With the accepted, early treatment of knee injuries by exploratory arthrotomy, the patient is given the best opportunity to escape the consequences of a suppurative arthritis. Furthermore, the later function of the joint is best assured by the early removal of all loose and foreign bodies. It should be emphasized that the after care of these wounds is very important. Much of the future function depends on the proper management of such patients at the Base Hospitals. Assuming that the knee wound has been cared for primarily in the Forward Hospital, the wounded man is usually transportable to the Fixed Hospitals after the effects of the anesthetic have worn off. Actually, he reaches the Base any time between the second and eighth day after wounding. The authors were concerned with the after care of these patients in the Base Hospital.

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During the 35 months spent in Africa, Italy and France,* over 300 compound injuries of the knee joint were seen and treated. Accurate statistics are available on 244 cases seen in Italy and France. Almost all these patients had received their primary care in the Evacuation Hospital.

Historical.—During the early part of the African campaign, the lines of evacuation were long and complicated, so that the majority of the patients were seen late after wounding. By the time the occasional patient with an infected knee joint reached the Base, a pyarthrosis had already developed. Unfortunately, no accurate figures are available on the penetrating wounds seen during the African campaign. In general, however, the initial surgery on penetrating wounds of the knee joint during this campaign consisted of the débridement of the wound, removal of the foreign body, and closure of the synovium. Some hospitals elected formal, exploratory arthrotomies, with closure of the synovium, even at this early date, but our records are too inadequate to draw any conclusions about the surgical principles employed in the Forward Hospitals. At the General Hospitals, the advantages of secondary suture of wounds were just being realized, and few knee wounds were actually sutured.

Septic joints with pyarthrosis were treated by bipatella incision, removal of the foreign body, irrigation of the joint space, and immobilization in a plaster hip spica. The synovium was held open by a pack which extended to, but not into, the joint. These patients usually had a stormy course and showed weight loss and other signs of chronic suppuration.

During the Italian campaign the management of wounds was changed radically. The program of secondary suture proved to be basically sound. Revolutionary advances were made in the management of soft-tissue injuries, but even greater was the advance in the methods of handling wounds of the knee joint. Whereas treatment of wounds early in the war was passive, and consisted principally of immobilization in plaster to avoid spreading infection, the program in Italy was changed to an active one, designed to control and eliminate infection and to restore function as early as possible. In the care of knee injuries, the early restoration of function is particularly important in order to avoid muscle atrophy and joint adhesions.

During the months of static warfare on the Cassino front in Italy, the Forward Hospitals reached a degree of excellence in the performance of débridements that has not since, in our opinion, been duplicated. The clean surgical wounds seen at the Base were most suitable for closure, and the entire program was facilitated. The value of routine, early arthrotomy became evident, but the procedure was not universally accepted during the early part of the Italian campaign.

The widespread use of penicillin as an aid in combating wound infection dates from the Spring of 1944. With the introduction of this new chemotherapeutic agent, the approach to reparative care of all types of wounded became

* The 21st General Hospital operated in North Africa from January to November, 1943, in Italy from January to September, 1944, and in France from October, 1944, until September, 1945.

more active. The conservative attitude toward treatment of knee joints with complicating infection changed to a more aggressive surgical approach. This viewpoint will be presented in Study II, based on this same series of 244 cases. The present paper is concerned with the early care of uninfected compound injuries of the knee joint. Although the conclusions are based on experience with battle injuries of the knee, they are also applicable to injuries of the knee seen in civilian surgery.

Care of Joint Injuries at the Base Hospital.—When received from the Forward Hospital, the patient with an adequately treated wound of the knee is comfortable, although he may have some fever if the period since wounding is short. He has had the benefit of arthrotomy, the joint has been débrided, the synovium closed, penicillin injected locally, the wound dressed, and the extremity immobilized in a long leg plaster encasement or Tobruk splint. A hip spica is preferred in the presence of severe bone injury. After correction of secondary anemia, and with the continuation of parenteral penicillin therapy, the patient is taken to the operating room, where facilities are available for formal arthrotomy. The plaster and dressings over the wound are removed. It is important that the original dressing should not be changed until this time, as repeated dressing of the wound leads only to secondary contamination and suppuration. If penicillin is instilled repeatedly at the Forward Hospital, it should be done without disturbing the dressings over the wound proper. After removal of the dressings in the operating room, the knee is inspected and tested for increased fluid, and most important, tested for pain on motion of the joint. The patient must necessarily remain awake during this portion of the procedure. The uninfected knee will have a small range of painless motion, whereas the infected knee joint is painful to even minor degrees of motion. It must be pointed out, however, that excessive ranges of motion, even in uninfected joints, will be painful. The patient is then anesthetized. If fluid is present, the joint is aspirated, the fluid examined grossly, and specimens taken for smear and culture. Gentle irrigation with saline through the aspiration needle is performed and the character of the returning fluid is carefully noted. The infected joint with leaking synovium will be apt to discharge flecks of purulent material with the irrigating fluid. If definite indication for arthrotomy exists, it should be done without delay, and with the aid of a pneumatic cuff tourniquet in order that the visualization of the joint be unimpaired. Usually, the joint which has received proper care in the forward area will need no further intra-articular surgery. Ten or twenty thousand units of penicillin in 10 to 20 cc. of saline are instilled into the synovial cavity. The skin, left unsutured in the Forward Hospital, is closed by simple suture. Systemic penicillin consisting of 25,000 units every three hours is continued from the time of admission to the Base until the knee wound is healed.

Immobilization.—The ordinary uncomplicated knee injury is usually immobilized in extension in a Tobruk splint. The principle of traction as well as immobilization is utilized by this type of splinting. Suppurating knee joints are immobilized in plaster hip spicas. However, it would seem that the type of

immobilization is not as important as the operative procedure in attempting to arrest the suppurative process within the joint. The real victories over infected joints rest in thorough exploration of the joint and removal of the cause or causes for suppuration.

The uncomplicated knee joint may require a second local instillation of penicillin, but usually the single instillation at the time of secondary suture is considered adequate. If indication for other injections arises, these may be done through a window in the encasement. The ordinary case without severe fracture is immobilized for about five to seven days after operation at the Base. Those cases where complication has occurred should receive daily local instillations of penicillin until the effusion has subsided and the temperature is receding. The systemic use of penicillin is continued also. Cases which respond favorably will generally show marked improvement in two or three days, the effusion subsiding gradually. The amount of periarticular swelling is sometimes surprising and becomes evident as joint effusion disappears. In the absence of major bone or soft-tissue damage, the plaster encasement is removed and gentle motion is started a few days after symptoms have subsided. No immobilization is used thereafter.

There is a minimal period during which the patient with a wound of the knee joint should be followed at the Base, and during which he should be considered nontransportable. This period is about three weeks in the average case. During this time, the skin should be closed, and quadriceps exercises and motion of the knee started. Evidence of suppuration or other complication, such as serious quadriceps atrophy or delay in moving the joint, is sufficient indication to prolong hospitalization in order to explore the knee or to supervise rehabilitation.

The keynotes in the after care of clean wounds of the knee are: First, the initiation of proper exercises as early as the first day after secondary suture of the skin to prevent quadriceps atrophy; and, second, the early mobilization of the joint to prevent the formation of adhesions that would restrict the range of motion. The latter is very important where the synovium has been destroyed at its lateral and medial reflections. For these reasons, the thoroughness of the initial care, aimed at preventing suppuration and smoothing articular defects, is probably the one most important phase in the proper care of compound injuries of the knee. It is only in those knee joints that have been properly cared for in the Evacuation Hospitals that early motion can be instituted.

Incidence of Complicating Fractures.—Bone injury was recorded in 168 of the 244 penetrating and perforating injuries of the knee. Forty-four of the entire series, or 18 per cent, were severe comminuted fractures of one or more condyles. Fracture of the patella occurred in 49 of the 244 cases, an incidence of 20 per cent. Thirteen of the series of 49 fractured patellae had had primary excision of the patella in the Forward Hospital. One patient had had partial excision of the patella at the Evacuation Hospital. At the time of reparative surgery, three more of the fractured patellae were excised, and the above mentioned partial patellectomy was completed.

TABLE I

	No. of Cases	Percentage
Total compound injuries of the knee joint	244	100
Total number of wounded, with bony injury	168	67
Total number with severe comminuted fractures	44	18
Total fractures of the patella	49	20
Fractures of the patella treated by primary excision	13	
Fractures of the patella treated by secondary excision	4 (1 exc. comp.)	
Total fractures treated by patellectomy	17	7

Severely comminuted fractures of the patella with irregularity of the articular surface should be treated by total patellectomy in order to minimize the later development of traumatic arthritis and to prevent infection. If a major fragment of the patella remains as a single piece with good articular surface, it may be possible to leave this segment in place, after removing the comminuted fragments. This may then be secured to the ligaments by wire sutures, if necessary. Experiments by Cohn indicate that total patellectomy is to be avoided when possible. The patella or portion of the patella is left only when the under surface of the part remaining is perfectly smooth. Many fractures of the patella are incomplete. Curettage of the fractured area and débridement of the injured tissue about it may leave almost the entire articular surface of the patella intact. Infected comminuted bits of the patella were curetted in four of the 49 fractures in this series.

If the roentgenograms are not decisive, the under surface of the patella should be felt with the gloved finger at the time of reparative surgery or secondary suture. This is to be done even at the risk of contaminating the joint by going through the wound to reach it.

In a large majority of cases, bone injury to the condyles is minor in nature, consisting of either penetrating injuries of bone, chip fractures, or incomplete fractures. On the other hand, the seriousness of the injury is not to be minimized in view of the danger of suppuration in the joint. The usual injury involves either the medial or lateral condyle of the femur, because the surface exposed is much greater. At arthrotomy, with adequate exposure, the irregular defect in the condyle is evident. The foreign body may project above the surface, embedded in the bone, or the elastic articular cartilage may close over the defect and hide the missile. In every instance, the missile should be removed when operative removal is not difficult. Sometimes, the missile will have passed up into the marrow cavity and usually it does not reflect good judgment to attempt recovery in such cases. After extraction of the metal, the edges of the defect are irregular and must be thoroughly smoothed and trimmed. Loose pieces of articular cartilage may interfere with the future function by doubling outward into the joint to become trapped between the tibial and femoral condyles. It is very important for future function as well as for the control of early infection, that the joint be inspected for loose particles. The defect in the condyle should be carefully prepared so that the edges are smooth and no tags of cartilage remain.

The severely comminuted fracture of the knee presents a serious problem at times. These wounds may be produced by either bullets or shell fragments.

The outlook is more serious in the latter. None of the four bullet wounds of the knee with marked degree of comminution developed a suppurating joint. There were 35 severely comminuted fractures secondary to wounding by shell fragments, and of this number, 12 patients developed uncontrolled infections of the knee joint. If the joint does not become infected, one can either use skeletal traction to avoid shortening of the extremity, or immobilize the joint in plaster hip spica to await solidification of the fragments. The shattered joint with irregular surface will probably require fusion at some later time.

The joint that is open as a result of the loss of soft-parts is also a serious problem. If the soft-parts are avulsed to such an extent that the joint cannot be closed, there is usually bone loss as well, and saving the joint is useless. If, however, there is loss of soft-parts with preservation of the bony and cartilaginous structures, prevention of infection is desirable, and a plastic procedure should be tried in order to try to close the joint space. In ten cases of the present series, there was loss of soft-tissues to such an extent that closure of the joint by simple suture was not possible. In five of the ten cases plastic closure was attempted. (The remaining five cases were damaged beyond repair.) This can be done either by swinging a wide-base pedicle flap over the soft-tissue defect of the joint, or by undercutting a bridge of skin, leaving it attached at both ends and advancing it over the defect. In two cases of the five the results were excellent and infection, otherwise inevitable, was avoided. A third patient had some drainage from beneath the flap which was thought to be from an osteomyelitis of the femoral condyle. He was afebrile when evacuated and his final result is not known at this time. Two cases must be regarded as failures, as both joints continued to drain along the borders of the flap. Flap closure is certainly to be tried in all those cases where enough of the bony parts remain to warrant an attempt to save the articulation. Such flap procedures are probably best done in the Forward Hospitals at the time of débridement. The delay in reaching definitive surgery is sometimes so great that irreparable damage is done to exposed articular surfaces before the joint is converted into a closed cavity.

The Italian and French campaigns have afforded an excellent opportunity to study the merits of routine early arthrotomy. During the early phase of the Italian campaign, 99 compound injuries of the knee joint were treated. Of these 99, only 32 had been subjected to formal arthrotomy at the time of initial care. In 60 cases, either débridement alone had been done, or, in some few cases, the foreign body had been considered small enough to leave in, or adjacent to, the joint. The records in the remaining seven patients are not clear.

With the invasion of Southern France, Colonel F. B. Berry, consulting surgeon to the 7th Army, directed that all wounds of the knee joint be subjected to formal arthrotomy. This directive was based on the experiences gained in Italy. The improvement in results was striking. One hundred and forty-five compound injuries of the knee were treated in France. Ninety-five of these had been subjected to complete exploration of the joint. The records in six other patients were inadequate. Forty-three patients had not been subjected to formal arthrotomy. (As patients reached us from other than the 7th

Army, the incidence of wounds débrided without arthrotomy increased.) The incidence of suppurating knee joints in the Italian series was about 16 per cent. In the French series, the over-all incidence was 9.6 per cent. However, the significant difference rests in those cases which were found to be septic on admission and which were amenable to secondary débridement of the joint. Of the 15 cases subjected to secondary arthrotomy as described in Part II, 12 were in the Italian series. Eleven of the 12 had not been subjected to formal arthrotomy in the Evacuation Hospitals. Of the three septic cases seen in France, and thought to be operable, all had been given the benefit of formal arthrotomy as part of the primary care. The reason for suppuration in these three cases was believed to be inadequate surgery. Suppuration in those joints with relatively minor cartilaginous and bony damage if left unchecked, is a much greater catastrophe than suppuration in a joint which will probably be nonfunctional due to severe fracture and irregularity of the joint surfaces. The significant difference between the series of routine, early arthrotomy and that of débridement of the soft-parts or simple removal of the foreign body lies in the reduced rate of infection in those cases where bony damage is minor and where preservation of a functioning joint is assured if infection can be circumvented.

Finally, a word should be said about the wounding agent. Table II shows the relative percentage in the present series:

TABLE II

	Number	Percentage
Wounded by shell fragment	188	77
Wounded by small arms	44	18
Wounded by questionable agent	12	5

It is significant that 27 of the 28 knees that were septic on admission were the result of shell fragment wounds. The one septic bullet wound in the series as shown in the last table of Study II, is open to question. One must logically conclude that the highly shattered knee joint caused by a bullet wound should be treated conservatively, since the probability is that the joint will not become infected. On the other hand, the minor degrees of bone injury secondary to bullet wound require arthrotomy, not so much to avoid infection as to assure later function of the joint by removing loose and partially detached bone and cartilage from the joint.

SUMMARY AND CONCLUSIONS

1. Results of the surgical care of 244 compound injuries of the knee joint are presented.

2. The history of the evolution of a standardized program of reparative surgery in these cases is given.

3. Details of the surgical approach to the noninfected wound of the knee joint are outlined, with stress on the local and general use of penicillin.

4. The importance of the detection of early suppurative arthritis of the knee should be emphasized and the value of the diagnostic sign of pain on motion of the injured knee is stressed.

5. Early mobilization of these injuries is necessary in order to prevent joint and quadriceps atrophy, as well as restricted motion.

6. The high incidence of patellectomy in this series (35 per cent of patella fractures) is thought to be justified in view of the possibility of subsequent infection or traumatic arthritis.

7. The lowered incidence of sepsis treated in this hospital during the French campaign is believed to be convincing evidence of the value of the surgical program outlined.

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(*To be continued*)

THE TREATMENT OF PERIPHERAL NERVE INJURIES COMPLICATED BY SKIN AND SOFT TISSUE DEFECTS

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The necessity for early surgical intervention in peripheral nerve injuries is now fully appreciated by the military neurosurgeon. Earlier in the war, concomitant injuries to the bones and soft parts received major consideration; reconstructive neurosurgery was instituted at the completion of bone healing. reconstructive bone surgery, and major plastic procedures.

When the Neurosurgical Center was organized at this hospital, the complicated problem of combined orthopedic-neurosurgical cases was recognized, and a subsection was created for the treatment of these cases. The expeditious treatment of patients in this subsection has proven its value; methods of approach and results are soon to be published.

The handling of neurosurgical cases with associated soft-part damage and loss of skin has presented similar difficulties. The patient-load in this category probably does not warrant the creation of a special subsection; however, the need of a plastic surgeon at a Neurosurgical Center is apparent.

The transfer of neurosurgical patients to Plastic Centers for preliminary surgery postpones nerve repair. Such plastic repair is often compromised by the neurosurgeon and an excellent cosmetic result jeopardized. Certain complicated plastic repairs requiring tube construction can best be handled at a Center, and delay in nerve repair has to be accepted unless preliminary neurosurgery can be done and split grafts utilized as a temporary measure.

However, the rotation of flaps and the construction of pedicle flaps can often be done at the time of nerve repair. Thus, the patient is submitted to but one procedure, and his nerve repair is not postponed. The prolongation in operating time is not a major consideration since local anesthesia is possible in most nerve repairs and in the smaller flaps. Thus far we have not used general anesthesia during the neurosurgery.

The first seven cases of a series have been completed. The neural lesion has been treated by accepted methods and an assay of regeneration is not pertinent to this paper. However, we believe that our experience in the combined management might be of interest to those confronted with these problems.

Scarred skin or split-thickness grafts necessarily mobilized in surgical procedures for restoration of nerve function often become ischemic, thus endangering the underlying neurosurgical repair and requiring secondary plastic procedures. As a prophylactic measure, these areas of doubtful vitality are excised at the completion of the neurosurgical procedures when the skin defect is covered by a pedicle flap. For defects of the upper extremity the pedicle is

raised from the trunk. Since the suture of nerve defects often necessitates immobilization of the upper extremity in a varying degree of flexion, the donor site is sometimes on the chest wall. If circumstances allow, it is better placed on the anterolateral aspect of the abdomen where the skin is loose, where there is more subcutaneous tissue, and where the defect remaining after raising the graft may often be closed primarily without distortion of topography.

Defects of the lower extremity have been covered by pedicle grafts raised from the other lower extremity. Here again, immobilization in flexion often limits the choice of the donor site. It often becomes necessary to use the posterior aspect of the upper or middle thigh, resulting in moderate postoperative discomfort for several days. The use of this area as a donor site makes it possible, however, to close the defect primarily, as in the trunk, whereas a similar area on the calf would require a split-thickness graft.

FIG. 1.—Case 1: Postoperative photograph of medial aspect of right leg showing healed full-thickness graft.

FIG. 2

FIG. 3

FIG. 2.—Case 2: Preoperative photograph of medial aspect of right ankle showing split-thickness graft overlying scar tissue.

FIG. 3.—Case 2: Postoperative photograph of medial aspect of right ankle showing healed full-thickness graft.

A preliminary survey and examination of each case is done jointly by the neurosurgeon and plastic surgeon. The latter decides upon the type of plastic procedure desirable, instructs the neurosurgeon in the pattern of scar removal,

FIG. 4

FIG. 4.—Case 3: Operative photograph showing skin defect due to excision of split-thickness graft and scar tissue. The neurorrhaphy has been completed, and the sutured nerve lies exposed.

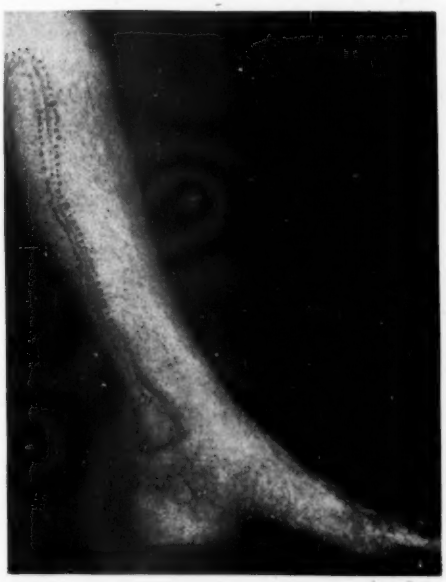

FIG. 5

FIG. 5.—Case 3: Postoperative photograph of the medial aspect of the left ankle showing the healed full-thickness graft.

and advises in the placing of the neurosurgical incision at the angles of the skin defect. Possible posturing of the extremity necessitated by the nerve repair is considered.

The neurosurgeon initiates the surgery under local anesthesia. The cutaneous scar or split graft is excised and the incision extended to permit of adequate exposure. The nerve is then repaired in the usual manner. It is

sometimes possible to transplant the suture site from the graft area (Fig. 7). If this is not feasible, it may be placed in a fresh muscle plane. We have not employed a tantalum sleeve in these cases; however, if the suture remains in a

FIG. 6.—Case 4: Preoperative photograph of right elbow. There is an extensive scar in large part immediately overlying bony tissue. A split-thickness graft had been utilized to secure early healing.

FIG. 7.—Case 4: Operative photograph showing pedicle graft in process of being sutured to the skin defect following excision of scar and split-thickness graft. The ulnar nerve has been transplanted anterior to the area of the pedicle graft.

moderately scarred bed at the site of the graft, a sleeve might be used. This should not be placed so as to underlie a suture line at the edge of the graft.

The recipient defect is carefully measured, and a gauze pattern is made with methylene blue. The outline of the pedicle graft is drawn with the dye by the aid of the pattern. In determining the length of the pedicle, due allow-

FIG. 8.—Case 4: Postoperative photograph of posteromedial aspect of right elbow showing healed full-thickness graft.

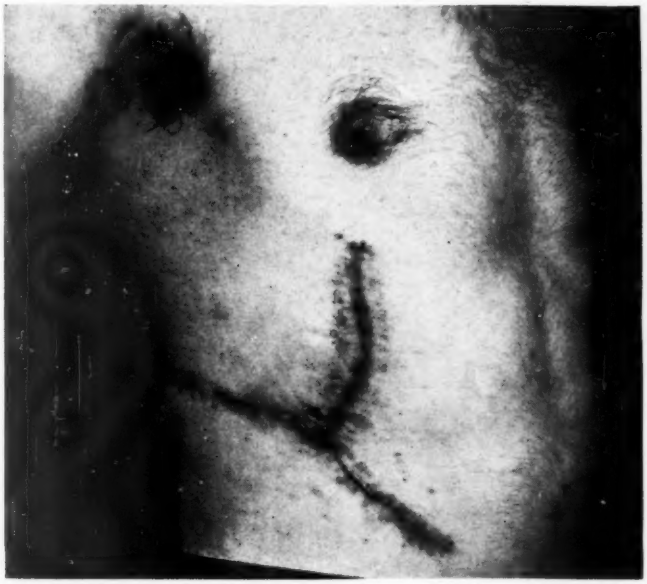

FIG. 9.—Case 4: Postoperative photograph of the trunk showing healed donor site.

FIG. 10.—Case 5: Preoperative photograph of right forearm showing extensive adherent scar following healing of battle wound by secondary intention.

FIG. 11

FIG. 12

FIG. 11.—Case 5: Postoperative photograph of volar surface, right forearm showing healed full-thickness graft.

FIG. 12.—Case 6: Operative photograph of the left hand and forearm showing skin defect due to excision of split-thickness graft and scar tissue. The neurorrhaphy has been completed.

ance is made for the distance between the abdomen and the base of the defect if they cannot be juxtaposed. The flap is raised to face either the flexor or extensor surface of the extremity according to the position of the defect, so that the abdominal wall is nearest its base. The full-thickness graft is raised at the level of the deep fascia. All donor areas thus far have been closed primarily. Our largest graft measures 15 x 10 cm. To facilitate closure, an incision is made on either side of and in line with the base of the pedicle, and triangular flaps are raised and rotated toward each other. After transection of the pedicle, revision of the wound of the donor area leaves a rather neat T-shaped scar. Silk technic is used throughout.

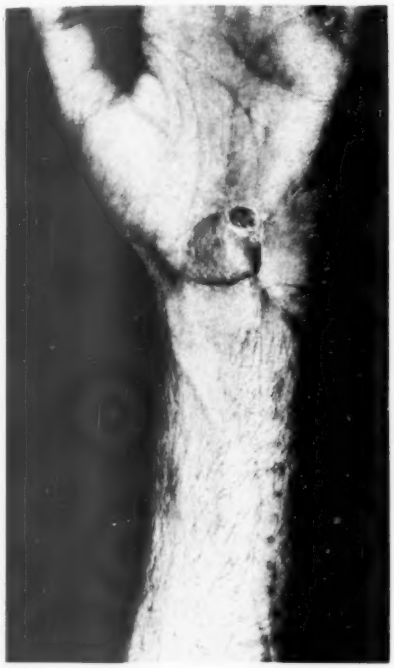

FIG. 13

FIG. 14

FIG. 13.—Case 6: Postoperative photograph of left wrist showing healed full-thickness graft.

FIG. 14.—Case 7: Preoperative photograph of right arm and elbow showing extensive deformity following loss of soft tissue.

It has been customary to transect the base of the pedicle in two, occasionally three stages. Transection has been completed in 15 to 21 days, depending on the width of the pedicle and the size of the graft as well as the circulatory appearance of the apex of the graft. A preliminary test by occlusion of the base with a rubber-covered intestinal clamp serves as a useful guide in determining the vascular independence of the graft. A proper amount of pressure is applied to the graft surface with a circular elastic bandage applied over mechanic's waste. Plaster of paris encasements have been used to secure immobilization until the graft has been freed from its source.

SUMMARY AND CONCLUSIONS

1. Peripheral nerve injuries complicating battle wounds of the extremities are often accompanied by soft tissue wounds which have been allowed either to heal secondarily or have been covered by split-thickness skin grafts.

2. Surgical defects resulting from removal of scar tissue of inadequate split-thickness grafts may be covered with full-thickness skin from pedicle grafts mobilized concomitantly with the neurosurgical procedure.

3. By combining these procedures definitive peripheral nerve surgery may often be completed earlier in the patient's convalescence.

FIG. 15.—Case 7: Preoperative photograph of lateral aspect of right arm and elbow showing extensive adherent scar overlying bone. The split-thickness graft has been used to secure early healing.

4. For defects of the upper extremity the abdominal or chest wall may serve as the donor site, for the lower extremity the surface of the opposite thigh may be used. The location of the donor site is often limited by the posturing necessitated by the neurosurgical procedure.

5. In most instances the defect created by raising the pedicle graft may be closed primarily by sliding flaps.

CASE REPORTS

Case 1

1. Date and type of injury:
   3 August 1944. Flak injury.
2. Extent of injury to (a) nerve, (b) skin and soft tissue:
   (a) Incomplete posterior tibial nerve paralysis, right.
   (b) Avulsion of skin and soft tissues lower third of right leg.

3. Previous operations (a) nerve, (b) skin and soft tissue:
   (a) No nerve surgery.
   (b) Wound healed by granulation in 6 months while a prisoner of war.
4. Reparative procedures (a) nerve, (b) skin and soft tissue defect:
   (a) 26 Nov. 1945—Neurolysis, posterior tibial nerve.
   (b) 26 Nov. 1945—Pedicle flap from posteromedial aspect of left thigh.
   5 Dec. 1945—Partial section of pedicle, local anesthesia.
   11 Dec. 1945—Complete transection of pedicle, revision of donor site, spinal anesthesia.
5. Results of plastic procedures:
   Graft healed without necrosis and without infection (Fig. 1).

FIG. 16

FIG. 17

FIG. 16.—Case 7: Postoperative photograph corresponding to Figure 14. Note correction of soft tissue deformity.

FIG. 17.—Case 7: Postoperative photograph corresponding to Figure 15. Note removal of scar tissue.

Case 2

1. Date and type of injury:
   7 January 1945. Mortar shell fragments.
2. Extent of injury to (a) nerve, (b) skin and soft tissue:
   (a) Incomplete posterior tibial and superficial peroneal nerve paralysis, right.
   (b) Avulsion of skin and soft tissues lower third of right leg with fracture, compound, comminuted, distal tibia.

3. Previous operations (a) nerve, (b) skin and soft tissue:
   (a) No nerve surgery.
   (b) 5 Feb. 1945—Split-thickness graft to defect (Fig. 2).
4. Reparative procedures (a) nerve, (b) skin and soft tissue defect:
   (a) 6 Dec. 1945—Neurolysis—posterior tibial nerve.
   6 Dec. 1945—Pedicle flap from posteromedial aspect of left thigh.
   12 Dec. 1945—Partial section of pedicle, local anesthesia.
   21 Dec. 1945—Complete transection of pedicle, revision of donor site, continuous spinal anesthesia.
5. Results of plastic procedures:
   Graft healed without necrosis and without infection (Fig. 3).

Case 3

1. Date and type of injury:
   17 March 1945. Shell fragments.
2. Extent of injury to (a) nerve, (b) skin and soft tissue:
   (a) Complete posterior tibial nerve paralysis, left.
   (b) Loss of skin and soft tissues. Laceration of posterior tibial artery and vein.
3. Previous operations (a) nerve, (b) skin and soft tissue:
   (a) 18 March 1945—Approximation of nerve ends with black silk.
   (b) 4 April 1945—Split-thickness graft to wound site.
4. Reparative procedures (a) nerve, (b) skin and soft tissue defect:
   (a) 27 Nov. 1945—Neurorrhaphy posterior tibial nerve, left.
   (b) 27 Nov. 1945—Pedicle graft from posteromedial aspect, right thigh (Fig. 4).
   6 Dec. 1945—Partial section of pedicle, local anesthesia.
   12 Dec. 1945—Complete section of pedicle, revision of donor site, spinal anesthesia.
5. Results of plastic procedures:
   Graft healed without necrosis and without infection (Fig. 5).

Case 4

1. Date and type of injury:
   26 December 1944. Shell fragments.
2. Extent of injury to (a) nerve, (b) skin and soft tissue:
   (a) Incomplete ulnar nerve paralysis, right.
   (b) Massive skin and soft tissue loss with fracture, compound, comminuted, of distal end of humerus (Fig. 6).
3. Previous operations (a) nerve, (b) skin and soft tissue:
   (a) No nerve surgery.
   (b) 19 January 1945—Split-thickness graft to right elbow.
4. Reparative procedures (a) nerve, (b) skin and soft tissue defect:
   (a) 12 Nov. 1945—Neurolysis and transplantation of right ulnar nerve.
   12 Nov. 1945—Pedicle graft from abdomen (Fig. 7).
   21 Nov. 1945—Partial section of pedicle, local anesthesia.
   29 Nov. 1945—Complete transection of pedicle, revision of donor site, inhalation anesthesia.
5. Results of plastic procedures:
   Graft healed without infection but with a spotty area of superficial necrosis in its distal third. This healed fairly promptly without in any way endangering the purpose of the graft (Fig. 8). Donor site healed *per primam* (Fig. 9).

Case 5

1. Date and type of injury:
   19 April 1945. Small arms fire.
2. Extent of injury to (a) nerve, (b) skin and soft tissue:
   (a) Incomplete paralysis of median nerve, right.
   (b) Skin and soft tissue loss with fracture, compound, comminuted, radius and ulna.

3. Previous operations (a) nerve, (b) skin and soft tissue:
   (a) No nerve surgery.
   (b) Wounds healed by granulation following débridement (Fig. 10).
4. Reparative procedures (a) nerve, (b) skin and soft tissue defect:
   (a) 24 Oct. 1945—Neurolysis median nerve, right.
   24 Oct. 1945—Pedicle flap from abdomen.
   1 Nov. 1945—Partial section of pedicle, local anesthesia.
   15 Nov. 1945—Complete transection of pedicle, revision of donor site, inhalation anesthesia.
5. Results of plastic procedures:
   Graft healed without necrosis and without infection (Fig. 11).
   4 Dec. 1945—Improvement in sensory and motor function permitting of neurosurgical clearance.

Case 6

1. Date and type of injury:
   28 April 1945. Small arms fire.
2. Extent of injury to (a) nerve, (b) skin and soft tissue:
   (a) Incomplete paralysis of ulnar nerve, left.
   (b) Avulsion of skin and soft tissues.
3. Previous operations (a) nerve, (b) skin and soft tissue:
   (a) 23 Oct. 1945—Exploration of ulnar nerve. No suture performed.
   (b) 5 May 1945—Secondary closure and split graft.
4. Reparative procedures (a) nerve, (b) skin and soft tissue defect:
   (a) 28 Nov. 1945—Neurorrhaphy and transplantation of left ulnar nerve (Fig. 12).
   (b) 28 Nov. 1945—Pedicle flap from left costal margin.
   7 Dec. 1945—Partial section of pedicle, local anesthesia.
   13 Dec. 1945—Complete transection of pedicle, revision of donor site, local anesthesia.
5. Results of plastic procedures:
   Graft healed after superficial necrosis of a small area (Fig. 13).

Case 7

1. Date and type of injury:
   17 April 1945. Shell fragments.
2. Extent of injury to (a) nerve, (b) skin and soft tissue:
   (a) Complete radial nerve paralysis, right.
   (b) Avulsion of skin and soft tissues lateral aspect lower third of arm. Fracture, compound, comminuted, humerus with loss of bone substance (Fig. 14).
3. Previous operations (a) nerve, (b) skin and soft tissue:
   (a) No nerve surgery.
   (b) 14 June 1945—Split-thickness graft to skin and soft tissue defect (Fig. 15).
4. Reparative procedures (a) nerve, (b) skin and soft tissue defect:
   (a) 23 Oct. 1945—Exploration of radial nerve. 8.5 cm. defect closed to 4 cm. by mobilization, patient is to have bone shortening at time of bone graft at a subsequent stage to permit of approximation of nerve.
   (b) 23 Oct. 1945—Pedicle flap from abdominal wall.
   31 Oct. 1945—Partial section of pedicle, local anesthesia.
   7 Nov. 1945—Partial section of pedicle, local anesthesia.
   14 Nov. 1945—Complete transection of pedicle. Revision of donor site. Inhalation anesthesia, ether.
5. Results of plastic procedures:
   Graft healed without necrosis, but with minor wound infection along the proximal suture line. This readily subsided and patient is ready for combined nerve suture and bone shortening (Figs. 16 and 17).

THE USE OF RADIOACTIVE SODIUM IN THE STUDY OF PERIPHERAL VASCULAR DISEASE*

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THE VIABILITY of an extremity depends upon blood delivered to it through the main and collateral arteries. Peripheral arterial disease affecting the walls of these vessels diminishes the local blood supply in different degrees with different types of pathology. It is very desirable in the treatment of peripheral vascular disease to have accurate information regarding the competency of the main and collateral arteries.

A procedure consisting of the introduction of radioactive sodium into the venous system, recording the time of its arrival at a part, usually the sole of the foot, and following the rate of accumulation of the material in that area, has been found useful in diagnosis, prognosis and evaluation of therapy in these cases. When this material is injected into a vein, it is rapidly mixed with the circulating blood. Since there is constant interchange of sodium between blood plasma and extravascular fluid, the amount of radioactive material in any region—*e.g.*, a foot—increases as it is brought there by the arterial circulation, passes through capillary walls and accumulates in extravascular fluid space. This increase continues until equilibrium is attained between intra- and extravascular sodium. The rate of increase and the final level attained depend upon the adequacy of the arterial circulation, the condition of the capillaries and the nature of the tissues. It has been found that the curve of the build-up to equilibrium can often be related to the degree of pathologic change in the vessels of the extremity.

Radioactive sodium (Na^{24}) is prepared in a cyclotron by bombarding sodium metaborate with deuterons. The metaborate containing the active atoms is dissolved in water, acidified with hydrochloric acid, and treated with methyl alcohol, resulting in the formation of methyl borate, sodium chloride and water. The solution is evaporated to dryness and heated, to destroy the pyrogens and to remove excess acid; the material is then dissolved in pyrogen-free distilled water, to give the desired concentration for injection, and autoclaved for one hour.[1] The radioactive atoms form a very small part of all the sodium in the solution, less than one in ten billion; the rest are the ordinary stable isotope. The two types of atoms are inseparable and indistinguishable until the radioactive ones disintegrate, emitting *beta* and *gamma* rays. A definite percentage of all the radioactive atoms disintegrate each second, and their disintegration can be detected by means of the Geiger-Müller counter.

In studies of peripheral vascular disease in the feet and legs, the patient lies on his back with his feet well-separated. The counter is placed against the sole of the foot (Fig. 1), and a measured amount of radioactive sodium, usually

* Aided by a grant from the Lilla Babbitt Hyde Foundation.

about 100 microcuries, in 3–7 cc. of sterile normal saline, is injected into an antecubital vein. Precautions are taken to see that all of the material gets into the vein and that neither the patient nor the injector is contaminated by it, if the latter is going to handle the counter. The times of the beginning and end of the injection are noted. Registration of the arrival of the radioactive material at the sole of the foot is made by an audible signal from a Geiger counter, with

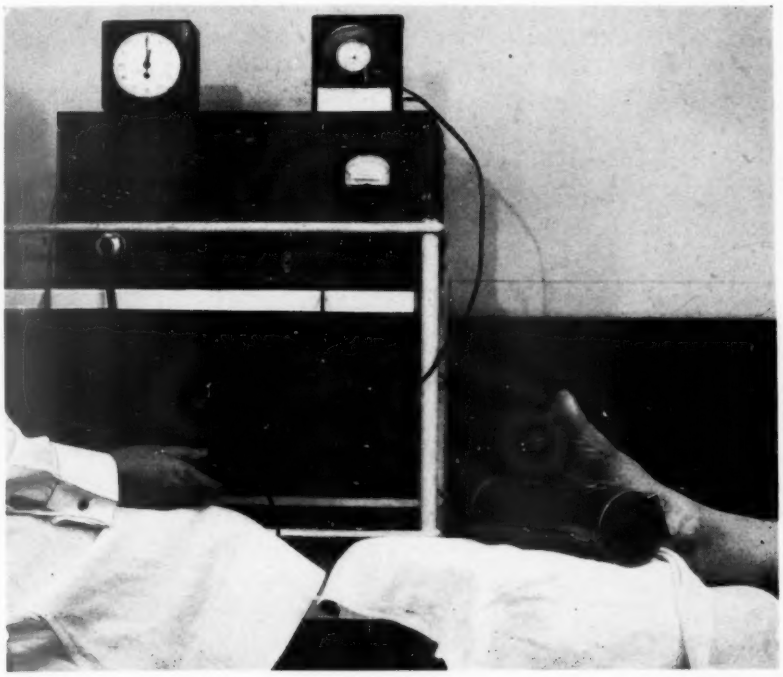


FIG. 1.—Geiger-Müller counting tube and scaling circuit. The shielded tube is shown in position against the foot of a patient.

an adjustable circuit so that the counting rate can be kept at a convenient level. Before injection there is a low background count due to cosmic rays and the presence in the vicinity of the apparatus of the radioactive material to be injected. When this material traverses the circulatory system and reaches the foot the counting rate increases sharply; in this manner the actual arm-to-foot circulation time can be measured. As the radioactive sodium leaves the capillaries and enters the extravascular fluid, build-up to equilibrium is manifested by the increase in counting rate. The "build-up curve" is plotted in counts per minute for 30–45 minutes, starting immediately after the injection.

Normals: This procedure has been carried out in 25 young normal individuals without clinical history or laboratory evidence of peripheral vascular disease; their curves all fall within the region indicated as normal range on the charts.

Charts of patients with peripheral vascular disease may fall below, within or above this range. Charts 1 to 6 record findings in various types of such

diseases, selected from some 300 patients who have been studied. In every instance the solid symbols represent counts at the sole of the right foot and the open symbols counts at the left foot.

ARTERIOSCLEROSIS

Each of these three patients had symptoms of several years duration. None had elevated blood pressure, and in none was the posterior tibial or dorsalis pedis artery palpable. All show curves somewhat below normal, except for the right foot of the case indicated by triangles (Chart 1).

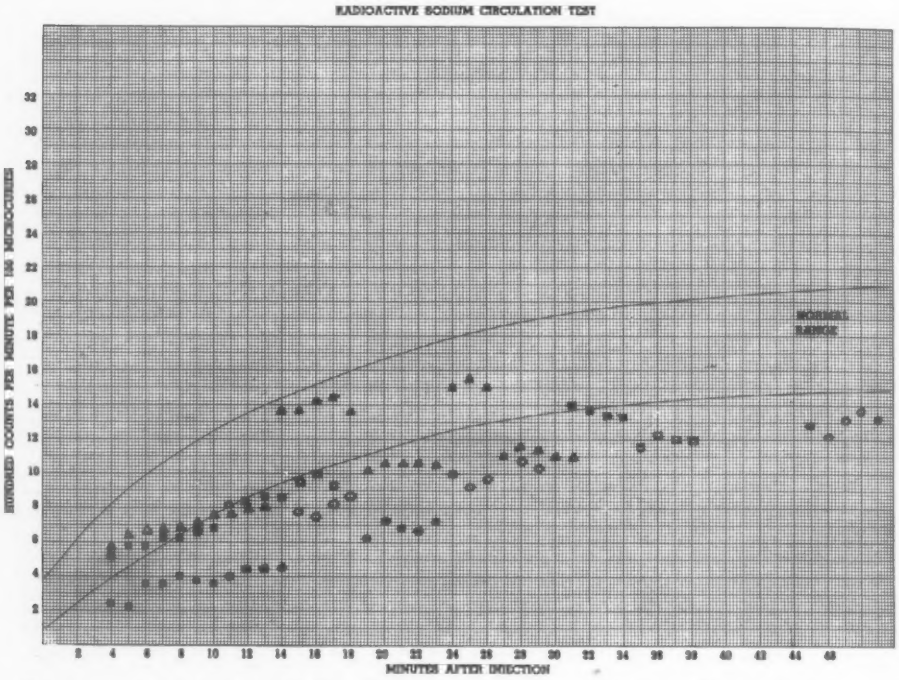


CHART 1.—*Arteriosclerosis:* For discussion of curves, see text. Closed symbols, counts against right foot; open symbols, counts against left foot.
Circles: Patient E. W.
Triangles: Patient B. C.
Squares: Patient A. S.

Circles: P. H. Unit No. 777381, E. W., a female, age 30, clinically improved on physiotherapy. The range of her reading in the absence of palpable main peripheral vessels indicates that her collateral circulation is reasonably well-established.

Triangles: P. H. Unit No. 722883, B. C., was a male, age 58, complaining of excruciating pain in both feet when they were dependent, and inability to walk. The left was worse than the right; he was incapacitated. Popliteal and femoral arteries were palpable: oscillometric readings extremely low. A modified guillotine amputation through the junction of the middle and lower third of the left leg was done, the stump healed by primary union. The arterial pathology of the specimen showed marked subintimal thickening in all arteries with occlusion and recanalization of the posterior tibial in the lower third of the leg. Three months later a similar amputation was performed through the right leg. The wound healed by primary union, and the pathology in the arterial

walls was identical with that of the left. The patient is using two artificial legs successfully. This patient's isotope curves are almost normal. The high readings on the right were due to mild inflammatory reaction. This degree of circulation was almost entirely the result of collateral, and was sufficient to permit primary healing following amputation. In the absence of pathology in the nerves of the amputated specimen, it appears that his exquisite pain was the result of local anoxia. This is the type of case in which the isotope curve indicated the probability of primary wound healing at the amputation site *below the knee.*

Squares: P. H. Unit No. 621627, A. S., was a male, age 40. This patient also had generalized xanthomatosis, with a serum cholesterol of 840 mg. per cent. No vessels were palpable in either extremity and oscillometric readings were very low. He has improved under physical therapy. Since the isotope study was made he has had a local thrombotic

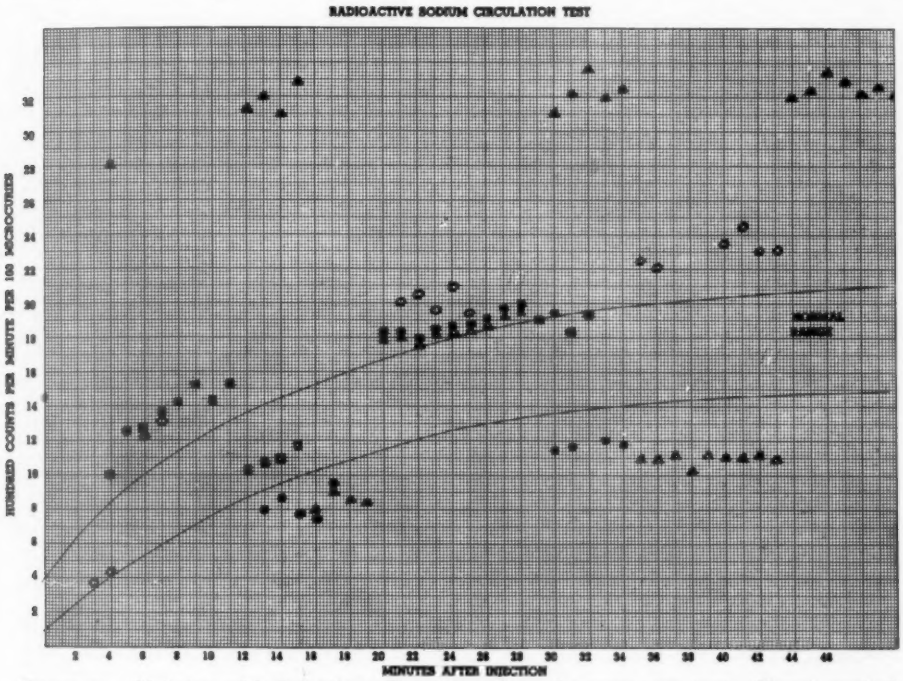


CHART 2.—*Diabetes with Infection:* For discussion of curves, see text. Closed symbols, counts against right foot; open symbols, counts against left foot.

Circles: Patient A. M.
Triangles: Patient E. G.
Squares: Patient A. P.

episode involving the dorsum of his right foot and three toes. He was treated conservatively, since his curve indicated adequate blood supply. In the absence of palpable main vessels, this was essentially all due to well-developed collateral circulation. On admission, he could not walk 100 feet; he can now walk slowly four miles.

DIABETES WITH INFECTION AND ARTERIOSCLEROSIS

These patients had moderate to severe diabetes of several years standing; all had serious infection in one foot. In all of them the counts at the infected foot were higher than normal, indicating good blood supply. Because of this, local surgery (amputation of toes) was carried out rather than amputation of the entire foot. Healing followed in all cases (Chart 2).

Circles: P. H. Unit No. 584036, A. M., was a female, age 61. Some time previous to the test she had had gangrene of the toes of the right foot, which had been amputated and healed. At the time of the study she had a cellulitis of the left second toe; the high readings indicated good blood supply, the toe was amputated and healed. Oscillometric readings were very low; there were no palpable arteries below the popliteal, the main digital vessels were thrombosed with calcification of their walls. The ample blood supply was due to well-developed collateral circulation.

Triangles: P. H. Unit No. 761577, E. G., was a female, age 63; osteomyelitis of right tarsus and fifth and third metatarsals, with swelling and cellulitis. Her main vessels were palpable. Material from a discharging sinus cultured a *Staphylococcus aureus* which was susceptible to penicillin. The very high radioactive sodium count indicated good blood supply and a favorable prognosis for conservative therapy. Sequestrectomy was done through small wounds, and an intensive course of penicillin established. The sinuses healed. The patient has been ambulatory for a year and a half with no complications.

Squares: P. H. Unit No. 639584, A. P., was a female, age 58; hepatosplenomegaly with diminished liver function, bilateral varicose veins and gangrene of the sole and toes

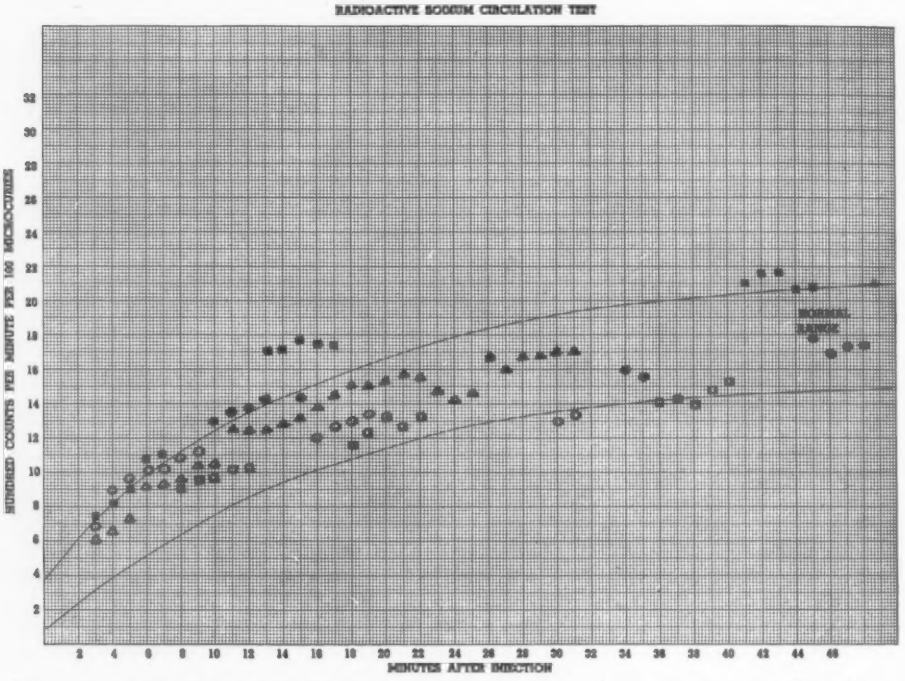
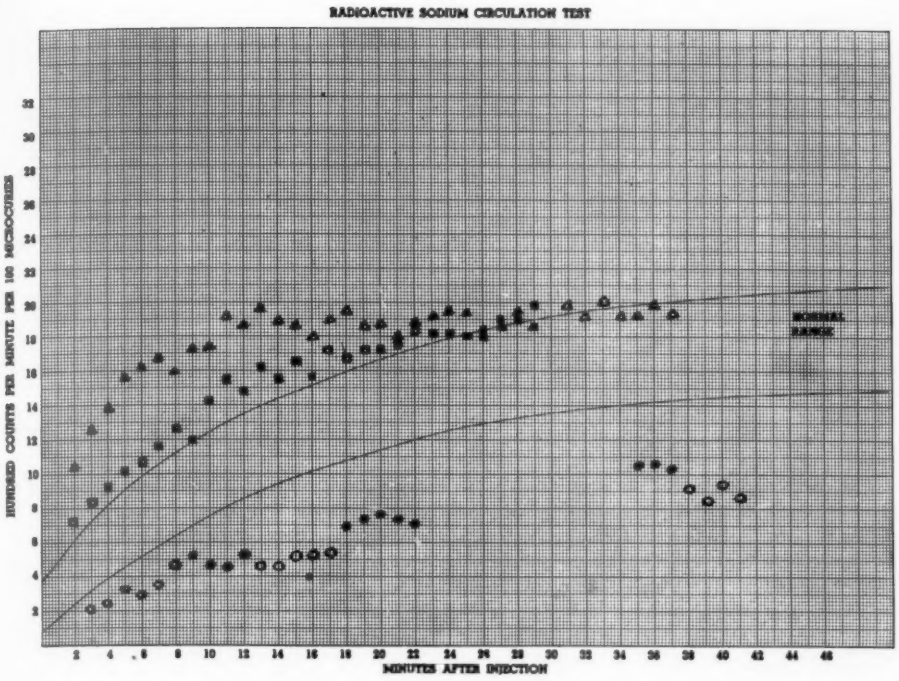


CHART 3.—*Thrombo-angiitis Obliterans:* For discussion of curves see text. Closed symbols, counts against right foot; open symbols, counts against left foot.

Circles: Patient R. S.
Triangles: Patient J. I.
Squares: Patient A. H.

of the left foot, following a burn from a hot water bottle; main vessels were palpable as far as the posterior tibial; the foot was completely anesthetic, due to diabetic neuropathy. An *hemolytic micro-aerophilic Streptococcus* and penicillin-sensitive *nonhemolytic* and *hemolytic Micrococci* were cultured from sloughing subcutaneous tissue. In view of the high count, local surgery was performed, the toes being amputated. (All surgery was performed without anesthesia.) An intensive course of penicillin was given. Healing was complete.

A



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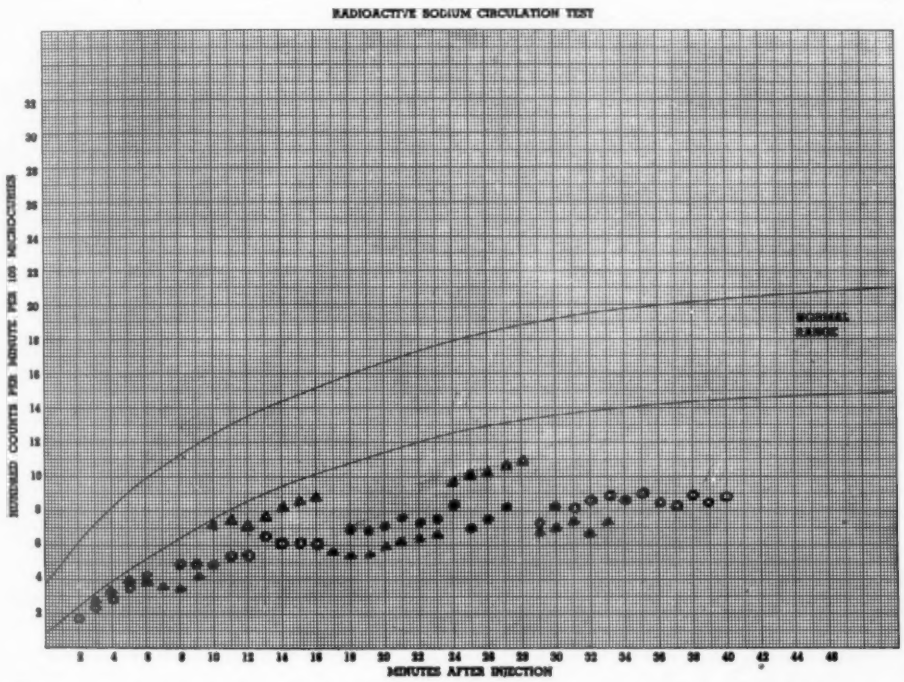


CHART 4.—*Hypertension:* For discussion of curves, see text. Closed symbols, counts against right foot; open symbols counts against left foot.

(A) Patient L. G.:
Circles: Before thoraco-lumbar sympathectomy.
Triangles: Three months after sympathectomy.
Squares: One year after sympathectomy.

(B) Patient A. S.:
Circles: Before sympathectomy.
Triangles: One year after sympathectomy.

THROMBO-ANGIITIS OBLITERANS

Two of these cases (one a woman) had active infection in one toe. The third had a spreading infection through his foot. All presented problems of treatment (Chart 3).

Circles: P. H. Unit No. 633731, R. S., was a female, age 30; gangrene of right great toe, associated with intermittent claudication of six months duration and multiple attacks of phlebitis. There was marked edema of the dorsum of the foot and exquisite pain. No arteries were palpable below the femoral, but the sodium curve in the high normal range indicated good collateral blood supply. Conservative surgery was done, consisting of amputation of the toe; healing occurred by secondary union, and there has been no further infection.

Triangles: P. H. Unit No. 44872, J. I., was a male, age 34. This patient had a history of six years duration; a peripheral novocaine crushing nerve block of posterior tibial, superficial peroneal and sural nerves of the left leg had been performed four years prior to the test; healing had been satisfactory. When studied, he had gangrene of the left great toe. With a sodium curve within the normal range, conservative surgery was expected to be successful; the toe was amputated and healed. There has been no further infection.

Squares: P. H. Unit No. 392546, A. H., was a male, age 38. Eight years before this study a novocaine and crushing nerve block had been done in the right leg, for relief of pain; an infected toe had healed. However at the time of the study the ulcer of the toe had recurred, and spread to the dorsum of the foot. The high count at the left foot indicated good blood supply but the spreading infection necessitated amputation of the leg at the junction of the lower and middle third. The wound is almost healed at present.

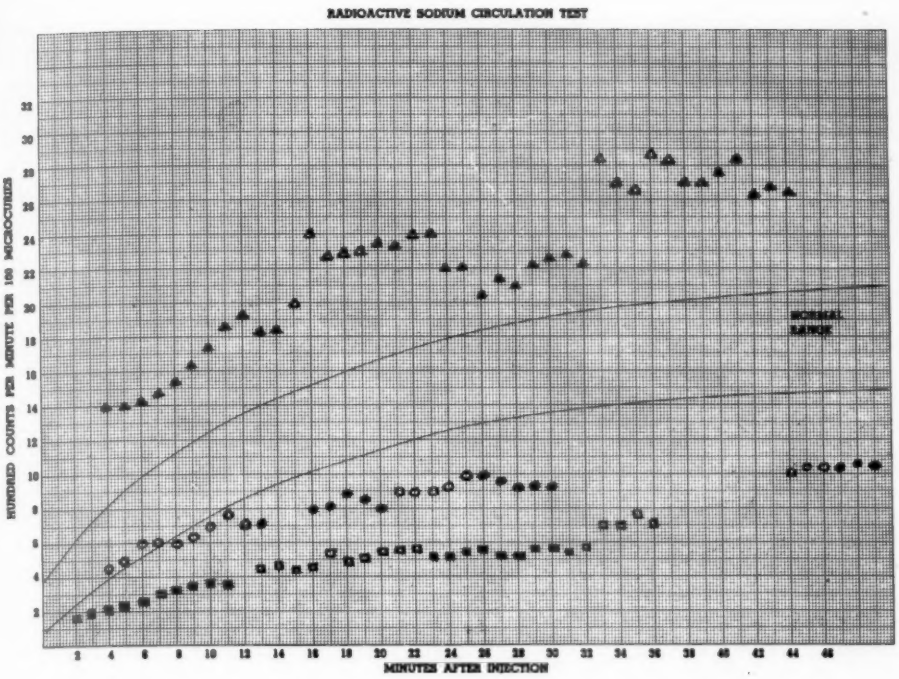
This is the type of case in which formerly amputation would have been performed above the knee because of uncertainty as to blood supply to allow for healing at a lower level.

HYPERTENSION

The problem of hypertension deserves especial attention in connection with the radiosodium studies. Patients fall into three groups, with curves very low, somewhat low, and nearly normal. These respond differently to thoracolumbar sympathectomy. Those with very low counts before operation usually do well; they are relieved of symptoms, either with or without marked drop in blood pressure. The postoperative curve is well above normal. This indicates that the low first curve is due largely to peripheral spasm; when this is relieved vaso dilatation results. Most of the patients whose count is nearly normal before operation have either experienced severe vascular complication soon after operation or have died. Those in this group appear least likely to be benefited by this type of surgery. The middle group, those with moderately low initial counts, need further study; as they respond differently to surgery (Charts 4A and B).

Chart 4A: P. H. Unit No. 772853, L. G., was a male, age 40; B. P. 270/160; symptoms for two years; Grade 2 hypertensive retinopathy. He was bedridden, with headaches, dyspnea, and palpitation. The circles show his preoperative curve. Three months following thoracolumbar sympathectomy he returned to work symptomless; the triangles show his curve at that time. A year later he is still without symptoms, although his pressure remains high. The squares show his present curve.

A



B

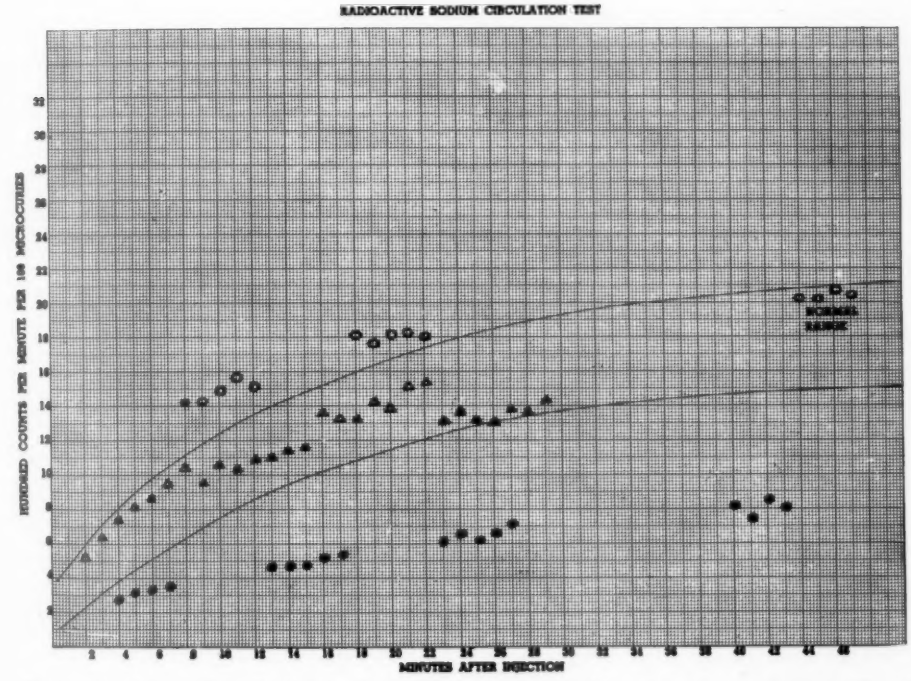


CHART 5.—*Immersion Foot and Frost-bite.* For discussion of curves, see text. Closed symbols, counts against right foot; open symbols, counts against left foot.

(A) Triangles: Patient E. M.: Frost-bite and infection.
Circles: Patient I. K.: Frost-bite without infection.
Squares: Patient J. W.: Immersion foot.

(B) Patient N. S.: Immersion foot.
Circles: One year after exposure; alcohol nerve block on left.
Triangles: Two and one-half years after exposure; alcohol nerve blocks on both sides.

Chart 4B: P. H. Unit No. 603879, A. S., was a female, age 40; B. P. 200/120; Grade 2 hypertensive retinopathy, advancing myocardial changes, no benefit from bed rest. The circles show her preoperative curve; the triangles show the situation two years later. She is asymptomatic; her pressure is 135/80. It was not possible to study her within the first year after the operation and there is no way of knowing whether she would have presented a high curve which returned to the lower range.

IMMERSION FOOT AND FROST-BITE

These patients usually have normally palpable arteries, but complain of pain on walking and of hypersusceptibility to cold. Their curves are low (Charts 5A and B).

Squares: No P. H. Unit No., J. W. (Chart 5A), 34-year-old seaman was examined in April, 1944, following a history of having been torpedoed in the northern Atlantic, February 23, 1943, and being in a life boat 17 days before rescue. During this time his hands and feet were frostbitten and he presented a typical picture of immersion feet from cold water. On examination, a year and one-half later, his extremities appeared perfectly normal; all of his arteries were normally palpable and his oscillometric readings were normal. He complained of pain only upon walking, in the soles of both feet, and of hypersusceptibility of both extremities to cold. His low curve indicates damage by cold with subsequent partial occlusion of the small arteries in the soles of both feet. This reading was the only objective laboratory finding in keeping with his clinical symptoms and upon the basis of it he was certified as not being fit for sea duty. There is no late follow-up on this case. Were it not for his low curve, this man would have been judged a malingerer.

Circles: P. H. Unit No. 419315, I. K., a 36-year-old male, froze his toes in 1934. This curve taken ten years later, indicates inadequate blood supply. The patient has had a coronary thrombosis, and probably now has peripheral arteriosclerosis, which may be worse because of the previous damage from freezing.

Triangles: P. H. Unit No. 777363, E. M., was a 39-year-old colored male. In 1940 his right foot was frostbitten and subsequently pain and ulceration developed in the great toe. This healed but reopened, and cultured a *nonhemolytic Streptococcus* and *Bacillus proteus*. The very high curve indicated patent main vessels, with inflammation, but it is not clear why the readings were also high in the uninvolved left foot. A partial amputation of the right great toe has been done, followed by a crushing nerve block because of persistent pain. The wound is still healing. The test will be repeated when healing is complete.

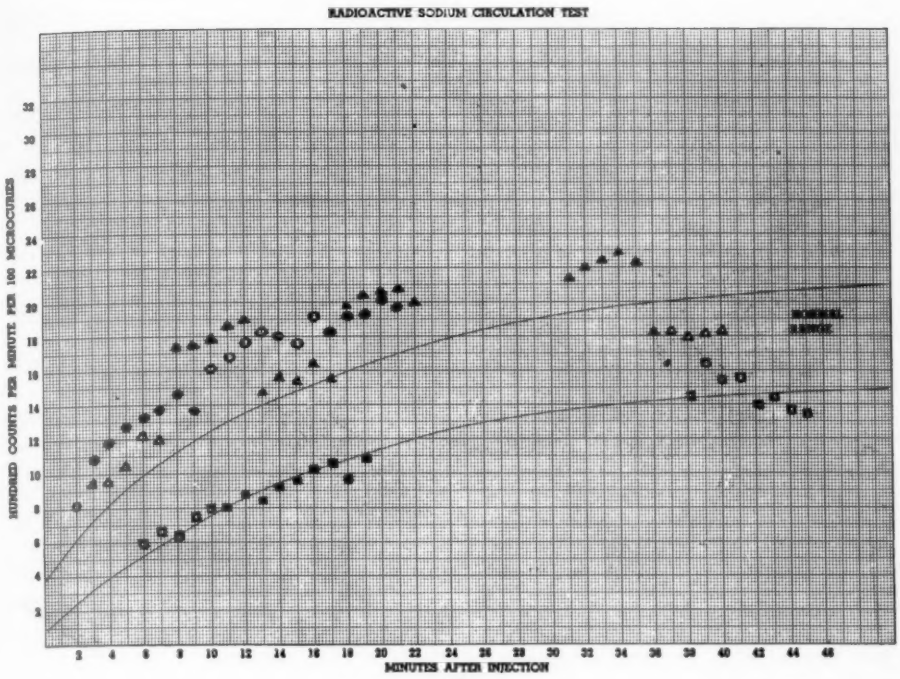
(Chart 5B), No P. H. Unit No., N. S., a 48-year-old Filipino steward, first seen in November, 1944, referred from the U. S. Marine Hospital for intolerance to cold and pain in feet, ankles, legs and knees. He had spent 19 days in an open life boat, subsequent to torpedoing of a ship in the South Indian Ocean in June, 1943. At the time of the examination, one year after exposure, the curve for the right foot was markedly low, while that in the left was above normal. He had had a left alcohol lumbar sympathetic block. These values are shown by the circles. The triangles give values obtained a year and one-half later, six months after a similar block had been performed on the right side. Both feet are now normal.

MISCELLANEOUS

Many cases which have been studied do not fall into well-defined disease groups. Nevertheless they warrant consideration as individual problems.

Circles: P. H. Unit No. 612902, A. D. (Chart 6A), was a white female, age 41. In 1940, she fell into a post-hole and her left leg became painful, blue, cold, and swollen.

A



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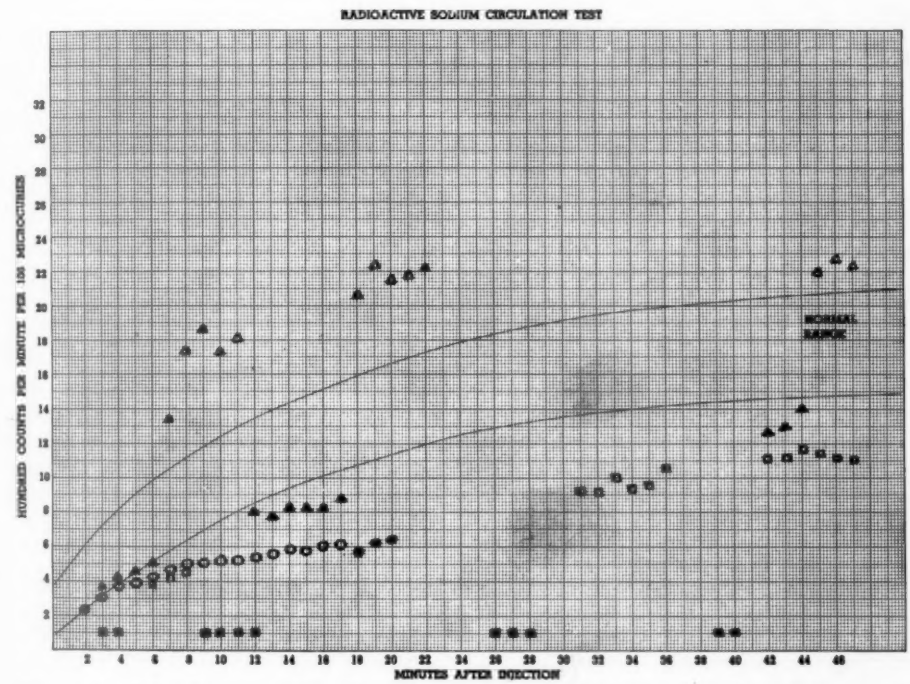

CHART 6.—*Miscellaneous:* For discussion of curves, see text. Closed symbols, counts against right foot; open symbols, counts against left foot.

(A) Circles: Patient A. D.: Accidental injury.
Triangles: Patient J. R.: Cavernous hemangioma.
Squares: Patient M. N.: Venous thrombosis.

(B) Triangles: Patient R. C.: Phlebitis.
Circles: Patient I. M.: Scleroderma.
Squares: Patient C. S.: Thrombosis of abdominal aorta.

Oscillometry was normal, roentgenograms negative, but function of the ankle joint was limited in all directions. Physiotherapy failed to relieve any symptoms. Following a left lumbar sympathetic novocaine block the temperature of this extremity rose 12° C. Accordingly, an excision of the left second and third lumbar sympathetic ganglia was done. The foot and leg became warm, all symptoms have disappeared, and the patient has returned to ambulatory occupation. It is to be regretted that a preoperative sodium study was not made. The postoperative curve is above normal for both feet. The high reading on the unoperated side suggests that some sympathetic fibers decussated and were destroyed by the operation on the left, thereby influencing the right.

Triangles: P. H. Unit No. 607824, J. R., was a Negro female, age 30, with a massive cavernous hemangioma of right inguinal region, buttock, thigh, and leg. The high reading on the affected side would be expected in view of large amount of extra blood in the leg.

Squares: P. H. Unit No. 555381, M. N., was a white female, age 33, with deep and superficial venous thrombosis of the right leg. The leg and thigh were so edematous that arteries could not be palpated. The normal sodium curve indicated that the block was not arterial, since the blood arrived there to deliver the material. Thrombophlebitic gangrene subsequently developed in both legs; the patient died. At autopsy, she was found to have carcinoma of the left intrahepatic bile duct, with carcinomatosis, and thrombi in many veins.

Triangles: P. H. Unit No. 803993, R. C. (Chart 6B), a male, age 38, sprained his right ankle, following which he developed phlebitis with pulmonary emboli. The femoral vein was ligated and found partly thrombosed. Sodium study at this time indicated adequate arterial blood supply in this leg. A modified guillotine amputation through the junction of the lower and middle thirds of the leg was performed, and the pathologic examination revealed a moderate degree of arteriosclerosis, with a calcification which had not severely compromised the lumen of any of the arteries. A generalized thrombosis and organization of all of the main arteries below the line of amputation had occurred. Some of the thrombi showed recanalization. Complete thrombosis of *all* deep and superficial veins in the leg and foot was present. At operation, not a single vessel was ligated. The wound healed by primary union, and the patient is wearing a prosthesis. The high sodium reading in the opposite extremity was probably due to inflammation there, which was clinically not detected until shortly after the study was made, when he developed phlebitis. The high count should have been a warning.

Circles: P. H. Unit No. 416356, I. M., was a male, age 29. Nine years before this study, a bilateral thoracolumbar sympathectomy had been done for Raynaud's syndrome. The benefit following this procedure was short-lived, the disease progressed to a typical generalized scleroderma, for which the patient was treated without success. The curve shows diminished blood supply. Death ensued six months later.

Squares: P. H. Unit No. 763262, C. S., was a male, age 44; thrombosis or embolus at bifurcation of abdominal aorta, with gangrene of both lower extremities, worse on the right. The extremely low reading at the right foot showed complete occlusion of all circulation, main and collateral, in this extremity. On the left, at the time of the test, some blood was being delivered. This later diminished, bilateral gangrene set in, and death ensued.

CONCLUSIONS

The use of radioactive isotopes as "tracers" has been found in many cases to supply a powerful new method for obtaining information of the status of the peripheral circulation. Radioactive sodium, introduced into a vein, is rapidly carried throughout all the blood vessels, and then passes through the capillary walls into the extravascular fluid. The arrival of the material at an extremity and the nature of its build-up there to equilibrium between intra-

and extravascular fluid can be followed with a Geiger-Müller counter. Curves plotted from these data give useful information regarding arterial blood supply to the extremity. By correlating this with clinical findings, conclusions can be reached regarding the degree of main or collateral circulation. In particular, estimates can be made of the degree of pathologic change in main or peripheral vascular disease.

Cases here presented indicate the manner in which the curves are used to determine when sufficient collateral circulation exists to warrant local conservative therapy. Similar studies at different levels of the leg have given valuable accurate information as to the site for amputation at which healing is to be expected. This has resulted in more amputations being done below the knee.

The group of essential hypertensives so far studied indicate a possibility that this test can be used to select cases which will or will not be expected to respond to thoracolumbar sympathectomy.

REFERENCE

[1] Smith, Beverly C., and Quimby, Edith H.: The Use of Radioactive Sodium as a Tracer in the Study of Peripheral Vascular Disease. Radiology, **45**, No. 4, 335–346, October, 1945.

THE VALUE OF EXTERNAL SKELETAL FIXATION IN ELECTIVE ORTHOPEDIC SURGERY

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THERE have been many articles in the literature in recent years on the use of external skeletal fixation in the form of the Stader splint, the Haynes and the Roger Anderson apparatus for the treatment of fresh fractures. Scanty are the reports on the use of such devices in elective surgery on the skeletal system.

Roger Anderson pins and apparatus have been used at this hospital extensively in the treatment of fresh fractures, but the purpose of this communication is to outline its usefulness as a method of fixation in definitive operations upon the bones and joints.

The following is a study of 57 consecutive cases in which external skeletal fixation was used. All but one of these cases was operated upon by the author. The additional case was added to make the variety of cases included complete. The list includes bone grafting, arthrodeses, and shortening of the humerus to permit radial nerve suture (See Table I). The bone grafting operations have been carried out with full-thickness onlay or inlay grafts. Many cancellous bone grafts have been done as well with this method of fixation but they are not included in this paper and will be reported later.

OPERATIVE TECHNIC IN GENERAL

The appropriate size of pin is used for each bone or joint. For bone grafting, $\frac{5}{32}$-inch pins are used for the tibia and femur, $\frac{4}{32}$-inch pins for the humerus, $\frac{3}{32}$-inch pins for the radius and ulna. For arthrodesis, $\frac{5}{32}$-inch pins are used for the ankle and knee joint; $\frac{4}{32}$-inch pins for the shoulder and elbow joint, and $\frac{3}{32}$-inch pins for the wrist joint.

The pins are inserted by a slow speed hand drill which eliminates thermal damage to the soft tissues and bone.

The pins must be inserted at the exact anatomic site dictated. This is important to minimize pin complications. The insertion of the pins is done before the skin incision is made in nearly all cases.

In bone grafting, two pins are used above and two pins below the fracture site. These are usually half-pin units, but in the femur the lower pin is a through-and-through pin, and in the tibia the upper and lower pins are through-and-through pins. After the fracture site has been exposed and freshened and the position is corrected, the fracture site is fixed in a "known" position by locking the clamps of the Roger Anderson apparatus. The self-aligning splint may be used to secure the reduction of the fracture site, but this is not necessary. The application of the onlay graft is then very easy. If a sliding inlay graft is used in the tibia or femur the graft may be cut with no difficulty, using

a motor saw if the pins are deliberately placed in the posterior cortex of the bone.

In arthrodesis, a different technic for each joint is used and will be described later.

Postoperatively, after the wound is healed, sterile gauze dressings securely wrapped around the pins are used. These are changed infrequently; since frequent dressings are unnecessary and there is danger of contaminating the pin sites. No plaster is used around the pins or around the extremity. The author does not believe this is useful.

Case Reports.—An example of each type of procedure listed in Table I is given. The majority of the cases had originally been compound fractures of the long bones in the shafts or involving the adjacent joints with or without previous osteomyelitis or septic arthritis. Most of the injuries were due to gunshot wounds. The indication for surgery in each case illustrated is fairly obvious from the roentgenographic appearance and a few words concerning the clinical condition preoperatively.

TABLE I

EXAMPLES OF EACH TYPE OF PROCEDURE

Procedure	Bone	No. of Cases	Average Period of Fixation
Bone Graft.....	Femur	10	20 weeks
	Tibia	15	18 weeks
	Humerus	8	14 weeks
	Radius	4	12 weeks
	Ulna	7	13 weeks
Shortening humerus.....		3	12 weeks
Arthrodesis (Joint):			
	Knee	4	14 weeks
	Ankle	2	16 weeks
	Shoulder	1	16 weeks
	Elbow	1	20 weeks
	Wrist	2	12 weeks
Total.....		57	

COMPLICATIONS

(1) *Pin Seepage:* This occurred in 12 cases, or 21 per cent of the total cases. Shaar and Kreuz have stated that: "The most serious objection to external fixation is the possibility of infection from the use of pins. We have had no infections from pins in 157 consecutive cases. One must, however, differentiate between ordinary pin seepage and actual infection about the pin sites. A small amount of seepage occurs in about 10 per cent of cases." The author is certainly in full agreement with this statement. They list a number of causes of pin seepage but it is felt that movement of the skin and soft tissue about the pin sites is the cause of pin seepage in nearly every case in this series. Skin tension following insertion of pins, if it occurs, is dealt with by a counter incision in the skin in the operating theater. Pins are always inserted through normal tissue.

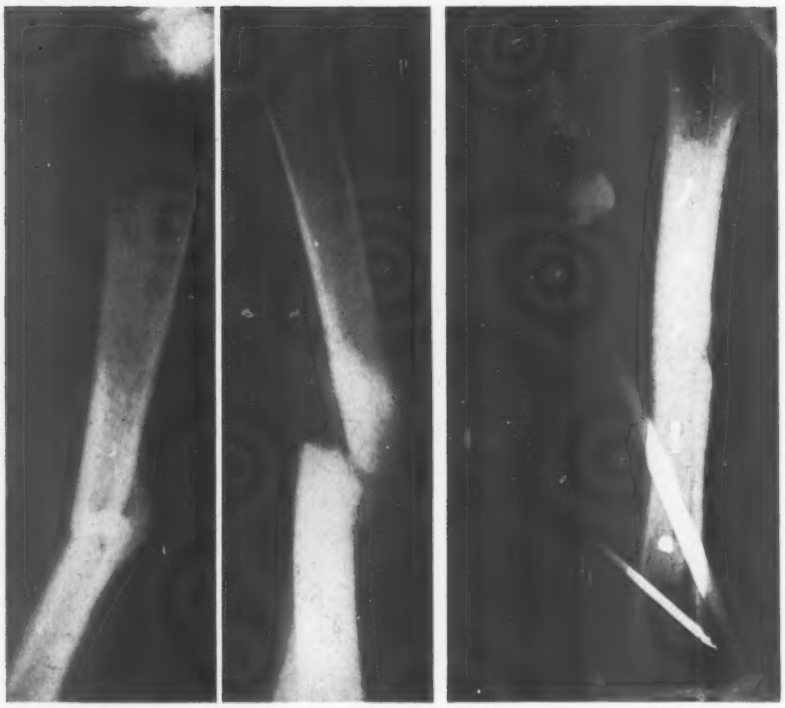

FIG. 1-A FIG. 1-B

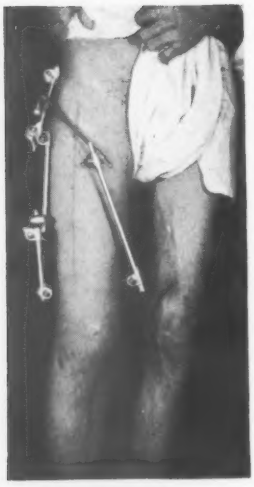

FIG. 1-C

SUMMARIZED CASE REPORTS

Fig. 1A.—Case 1: Shows the roentgenographic appearance of a compound fracture of the right femur after eight months' immobilization in plaster. Clinically, there was motion at the fracture site and 35 degrees external rotation of the distal fragment on the proximal.

Fig. 1B.—Case 1: Anteroposterior view of the femur 14 weeks after a tibial onlay bone graft with Roger Anderson fixation. Early union is present. Immobilization discontinued 18 weeks postoperatively.

Fig. 1C.—Case 1: Photograph of the same patient with external skeletal fixation apparatus.

FIG. 2-A

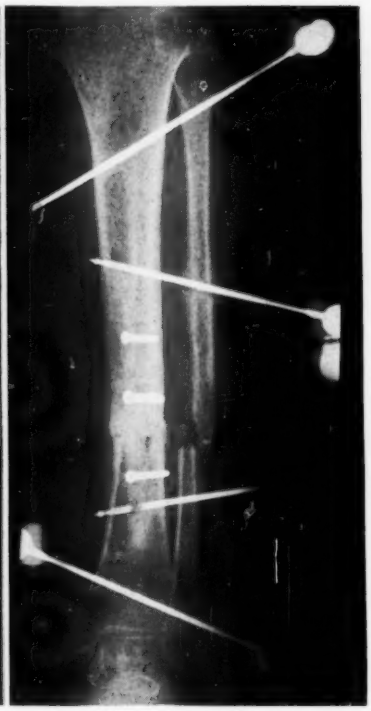

FIG. 2-B

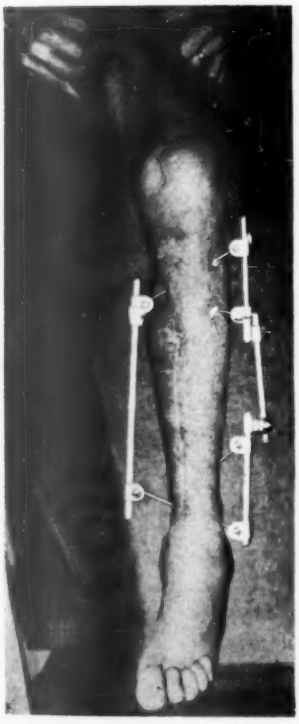

FIG. 2-C

Fig. 2A.—Case 2: Roentgenograms of a compound fracture of the tibia 10 months following gunshot wound. There had been continuous immobilization since this patient was wounded, including three months in a walking plaster. The skin wound had been healed for eight months.

Fig. 2B.—Case 2: Roentgenographic appearance 12 weeks after a sliding bone graft with additional cancellous bone from the opposite tibia. Immobilization discontinued in 16 weeks with union present.

Fig. 2C.—Case 2: Photograph of the patient after surgery.

FIG. 3-A

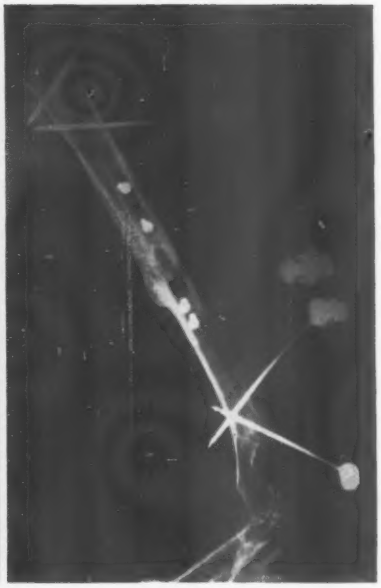

FIG. 3-B

Fig. 3A.—Case 3: Roentgenographic appearance of an original compound fracture of the humerus on arrival at this hospital following seven months immobilization. His wound was well-healed.

Fig. 3B.—Case 3: Fourteen weeks after a tibial onlay bone graft with additional tibial cancellous bone. Union is present.

Fig. 3C.—Photograph of a different patient who had also had a bone graft of the humerus with Roger Anderson fixation showing the position of the pins.

Fig. 3D.—Photograph showing range of abduction of the shoulder with external skeletal fixation apparatus six weeks postoperatively.

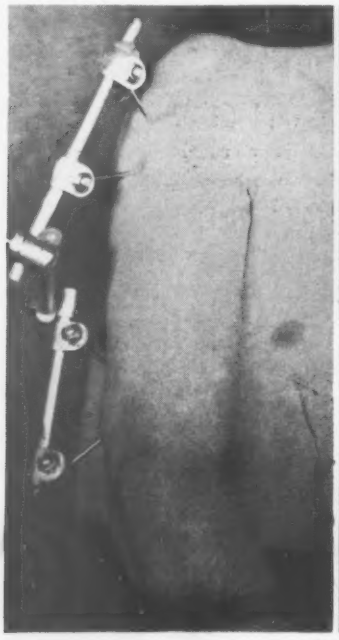

FIG. 3-C

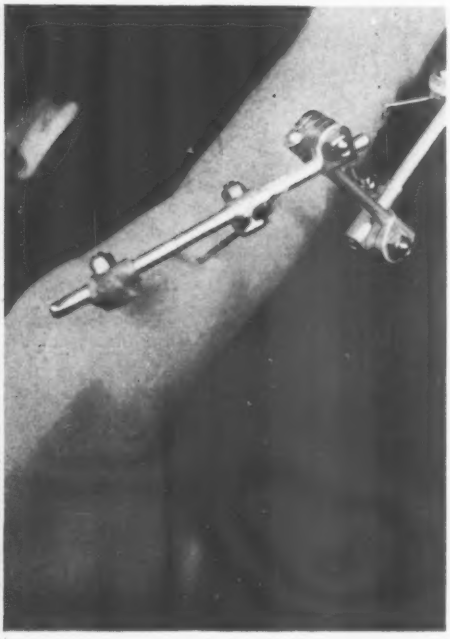

FIG. 3-D

FIG. 4-A

FIG. 4-B

Fig. 4A.—Case 4: Roentgenogram showing preoperative appearance of a gunshot wound of the forearm and fracture of the radius. This patient also had a median nerve lesion which had been explored and sutured previously.

Fig. 4B.—Case 4: Roentgenograms six weeks following tibial onlay bone graft with cancellous bone. The upper pin is not in the elbow joint in the oblique roentgenogram. Union occurred in 12 weeks.

FIG. 5-A

FIG. 5-B

Fig. 5A.—Case 5: Roentgenographic appearance of a fracture of the ulna which was ununited clinically. The fracture was three years old and one previous bone graft elsewhere had failed.

Fig. 5B.—Case 5: Roentgenographic appearance 12 weeks after tibial onlay graft. Union is present. The lower pin is not in the radius in oblique views. Rotation of the forearm was possible during the healing period.

Fig. 5C.—Photograph of a different patient's forearm with fixation apparatus following bone graft of the ulna.

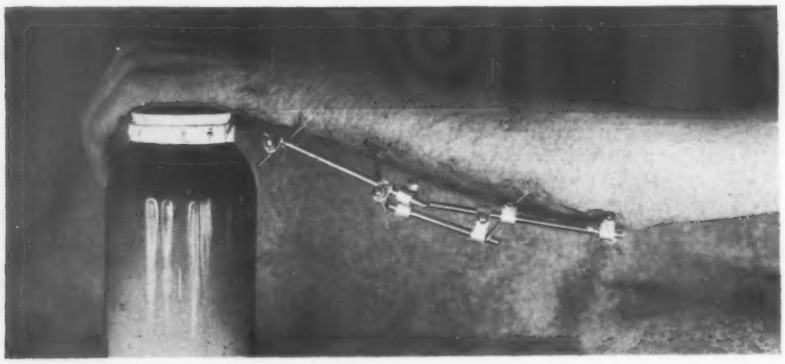

FIG. 5-C

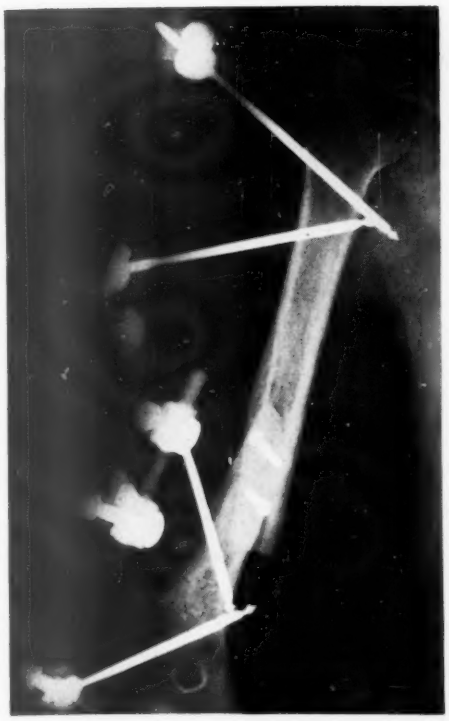

FIG. 6

Fig. 6.—Case 6: Postoperative roentgenogram of a shortening of the humerus of 6.5 cm. to permit end-to-end radial nerve suture. An oblique osteotomy was used. The angulation at the osteotomy site was present before the Roger Anderson apparatus was locked. Pins remained in the humerus 12 weeks, when union occurred. Subsequently, there was recovery in the muscles supplied by the radial nerve.

Fig. 7A.—Case 7: Roentgenographic appearance of knee joint to months following a compound fracture of the tibia (gunshot wound) involving the knee joint originally with osteomyelitis and septic arthritis.

Fig. 7B.—Case 7: Anteroposterior view of a surgical arthrodesis of the knee joint 10 weeks postoperatively. Early union is present. Immobilization discontinued in 14 weeks, when ankylosis was complete. Four $\frac{5}{32}$-inch pins are used and their position is clearly indicated in the roentgenogram. The two oblique pins cross through the knee joint. The articular cartilage is removed from opposing joint surfaces before these oblique pins are inserted.

FIG. 7-A

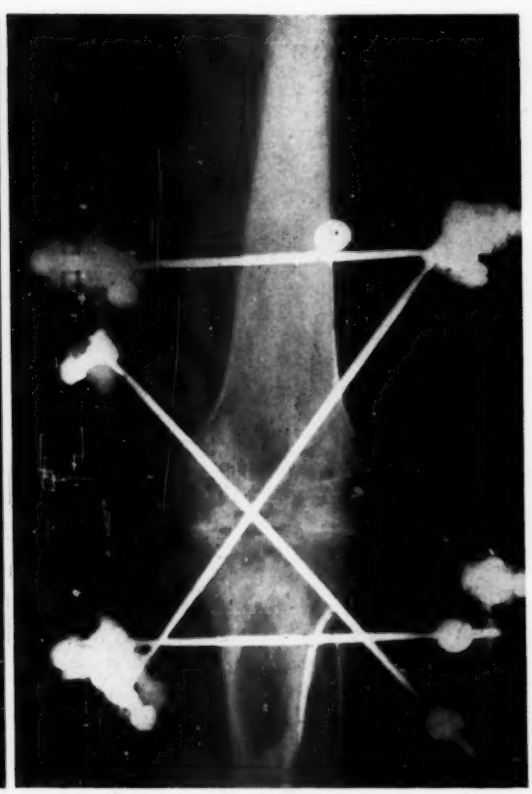

FIG. 7-B

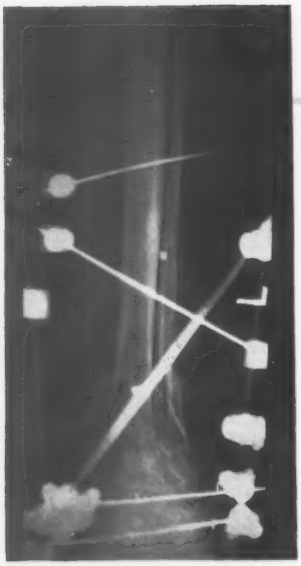

FIG. 8

Fig. 8.—Case 8: Postoperative roentgenogram of an arthrodesis of the ankle joint, with sliding tibial bone graft into the astragalus. This was a compound fracture of the lower tibia involving the ankle joint originally. Four 5/32-inch pins are used for fixation, two in the tibia and one each in the astragalus and calcaneus. The roentgenogram shows bony ankylosis of the ankle joint, which actually is fixed in 5 per cent of equinus.

Fig. 9A.—Case 9: Roentgenographic appearance of shoulder 18 months following gunshot wound. There was a neurotmesis of the circumflex nerve with complete deltoid muscle paralysis.

Fig. 9B.—Case 9: Appearance 10 weeks following arthrodesis of the shoulder joint with the use of a tibial bone peg driven through the upper humerus into the glenoid. External skeletal fixation. There are two 1/32-inch pins in the scapular spine, one through-and-through pin in the acromium and two half-pins in the humerus. Active motion in the elbow joint and scapulothoracic joints during pin fixation.

Fig. 9C.—Case 9: Roentgenographic appearance of the shoulder joint 16 weeks postoperatively showing solid bony ankylosis in 52 degrees of abduction. The humerus is in 30 degrees forward elevation at the shoulder joint.

FIG. 9-A

FIG. 9-B

FIG. 9-C

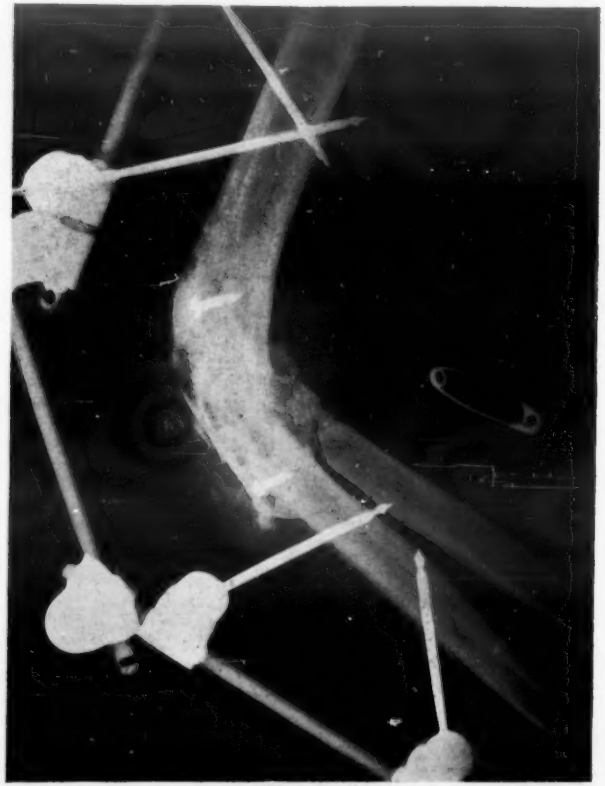

FIG. 10-A

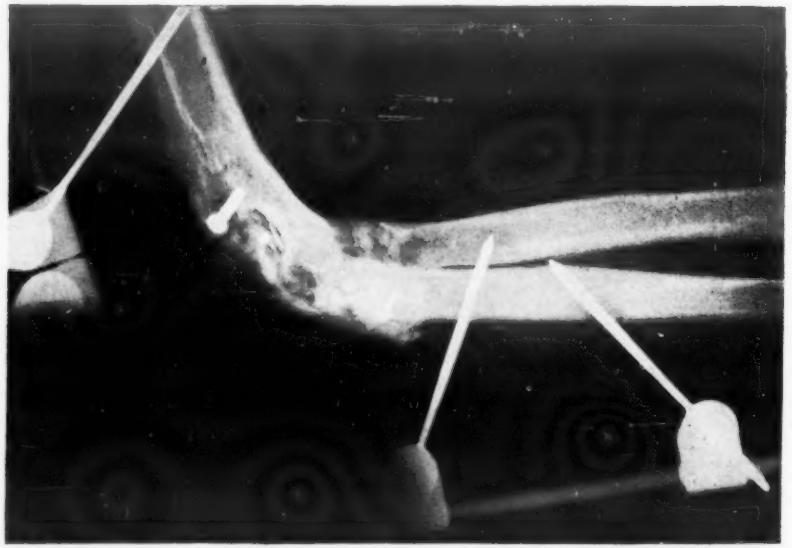

FIG. 10-B

Fig. 10A.—Case 10: Roentgenographic appearance of an arthrodesis of the elbow joint, with osteoperiosteal graft, two weeks postoperatively. Operation by Sqn. Ldr. F. P. Patterson, R. C. A. F. The position of the 1/32-pins are clearly shown in the humerus and ulna.

Fig. 10B.—Case 10: Roentgenographic appearance of elbow joint 20 weeks postoperatively. Solid bony anklyosis is present.

Fig. 11.—Case 11: Roentgenographic appearance of an arthrodesis of the wrist joint using an osteoperiosteal graft 12 weeks postoperatively. The indication for surgery was a posttraumatic arthritis of the radiocarpal joint following old ununited fracture of the carpal scaphoid. The position of the 3/32-pins are shown in the roentgenogram; three half-pins in the radius, one half-pin unit in the second metacarpal shaft and one half-pin unit in the fifth metacarpal shaft. Radial-ulnar movement is preserved during the healing period. Bony ankylosis is present.

FIG. 11

Pin seepage has never been serious and if local discomfort results, it is readily relieved by hot foments to the area for 24 to 48 hours. It most often occurred around the upper pin in the femur and humerus where the pin must penetrate a thick layer of muscle. To combat the problem in these locations it is helpful to insert the fixation pin slightly distal to the conventional position.

(2) *Pin Tract Infection:* This did not occur. In only three of the cases the pin sites did not heal in seven to ten days. All these three were completely healed in 15 days.

(3) *Osteomyelitis following Bone Penetration by Pins:* This did not occur.

(4) *Pin Sequestra:* None. Pins are inserted with a slow speed hand drill and this eliminates the element of thermal necrosis of bone.

(5) *Delayed Union and Nonunion following Bone Grafting:* There were no cases of nonunion. There were two cases of delayed union. One tibia required seven months to unite with continuous immobilization. This had been originally a compound fracture due to gunshot wound, with very poor bone substance at the fracture site as visualized at operation.

One femur in a mental case (schizophrenia) is not united nine months after operation. He had a severe wound infection postoperatively, with osteomyelitis. The infection is clearing at present and the graft is still bridging the fracture site. It appears that union will occur with further immobilization. It is to be noted that the infection at no time involved the pin tracts or the area of the femur which they penetrated. It was an infection of the operative site.

(6) *Exacerbation of Infection from Old Compound Wound:* This occurred

in four cases, without serious results. The operative incision was not affected. Bony union was not unduly delayed by this complication. In the four cases mentioned, the old wounds healed again in periods varying from three to eight weeks. This is not a high percentage when one considers the fact that in the series of 57 cases, 48, or 84.2 per cent, were originally compound fractures. Furthermore, elective surgery on bones and joints is being undertaken much earlier than the six to twelve months previously recommended, on cases which had originally been compound fractures due to gunshot wounds and were actually or potentially infected.

(7) *Postoperative Infection of Wound:* This was a case of a bone graft of the femur in a mental case which was discussed under "Delayed Union."

(8) *Renal Lithiasis:* No cases. Fractures of the femur and tibia and arthrodeses of the knee are ambulatory early.

SUMMARY

The advantages of external skeletal fixation when used in conjunction with bone grafting and arthrodeses are similar to those when this type of reduction and fixation is used in fresh fractures. We feel that Roger Anderson pins and apparatus are superior to other forms of external skeletal fixation for this purpose.

ADVANTAGES

(1) *Rigid and Continuous Fixation of the Fracture Site:* Plaster of paris encasements become loose and must be changed at intervals.

(2) *The Operative Procedure is Simplified:* Fixing the graft to the "host" bone is easier when the fracture site is held in a "fixed" position. Less fixation of the graft is necessary although this cannot be entirely dispensed with. Insertion of pins is much less exertion than applying a plaster encasement following the operation.

(3) *The Joints above and below the Fracture Site can be Mobilized:* This is done by physiotherapy to these joints during the healing process if they have been immobilized in plaster previous to surgery. Active motion of these joints is carried out postoperatively in all cases.

(4) *Early Ambulation is Provided* in the lower extremities except when a normal tibia is used to provide the graft for the injured tibia. Weight-bearing, with pins *in situ,* is allowed, commencing from eight to ten weeks postoperatively following operations on the lower extremities.

(5) *Minimal Nursing Care* is necessary for these patients.

(6) *Patients are Reasonably Comfortable:* In a survey of 20 patients who had been immobilized in plaster prior to surgery, 19 preferred the external skeletal fixation.

DISADVANTAGES

The disadvantages, of course, are the dangers of complications. These complications have been discussed. Although pin seepage was present in 21 per cent of these cases it was not a distressing feature and it can be minimized by precision in the placing of pins.